SEP 15 1944

VOLUME LIV AUGUST, 1944 NUMBER 8

Medical Library

THE LARYNGOSCOPE

FOUNDED IN 1896
BY
MAX A. GOLDSTEIN, M. D.

PUBLISHED BY
THE LARYNGOSCOPE
640 SOUTH KINGSHIGHWAY ST. LOUIS (10), MO., U. S. A.

NOTICE TO CONTRIBUTORS

THE LARYNGOSCOPE reserves the right of exclusive publication of all articles submitted. This does not preclude their publication in Transactions of the various Societies.

Manuscripts should be typewritten, double spaced, on one side of paper only and with sufficient margins to allow for corrections.

References should be complete: authors surname, initials, title of article, journal, volume, page, month, year.

Six illustrations will be furnished for each article without cost to author. Authors will please limit illustrations to six or assume the expense of additional illustrations.

Proofs will be submitted to authors for corrections. If these are not returned, articles will be published as corrected in this office:

Reprints will be furnished at the following prices:

WITHOUT COVER

	250 Copies	500 Copies	1000 Copies	2000 Copies
Four Pages	$ 5.75	$ 7.00	$ 9.50	$14.50
Eight Pages	12.00	14.50	19.50	29.50
Twelve Pages	17.00	21.25	30.00	47.50
Sixteen Pages	21.50	26.50	36.50	56.50
Twenty Pages	26.25	32.75	46.00	72.50
Twenty-four Pages	30.50	38.00	53.00	83.00
Thirty-two Pages	40.50	48.25	65.00	98.50

WITH COVER

Four Pages	$ 9.75	$12.50	$18.00	$29.00
Eight Pages	16.00	20.00	28.00	44.00
Twelve Pages	21.00	26.75	38.50	62.00
Sixteen Pages	25.50	32.00	45.00	71.00
Twenty Pages	30.25	38.25	54.50	87.00
Twenty-four Pages	34.50	43.50	61.50	97.50
Thirty-two Pages	44.50	53.75	73.50	113.00

Express charges to be paid by consignee.

THE
LARYNGOSCOPE.

VOL. LIV AUGUST, 1944. No. 8

ACOUSTIC TRAUMA OF THE ORGAN OF CORTI IN THE GUINEA PIG.*†

M. H. LURIE, M.D.; H. DAVIS, M.D., and
J. E. HAWKINS, JR., Ph.D.,
Boston.

In the past three years over 200 guinea pigs' ears have been exposed to sounds of high intensity and the organ of Corti studied for evidence of pathological changes. The experiments were both acute and chronic. In the acute experiments the cochlea was tested immediately after exposure or within two hours after exposure and the cochlea fixed in Heidenhain's Susa solution. In the chronic experiments the animals were allowed to live from two to 55 days after the exposure, then tested and the cochlea fixed for histological study.

The sources of sound used for the laboratory exposures were a Western Electric loud speaking telephone No. 598-B and the sound system at the Harvard Medical School, Department of Physiology. The 598-B was used for exposures at 500 cycles per second up to 157.5 dcb., at 1,000 cycles up to 148 dcb., and at 2,000 cycles up to 143 dcb. The intensity was measured before exposure by means of a sound level

*Read at the Seventy-seventh Annual Meeting of the American Otological Society, New York, June 6, 1944.

†Department of Otology, Laryngology and Physiology, Harvard Medical School and Mosher Laboratory, Massachusetts Eye and Ear Infirmary, Boston.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, July 1, 1944.

meter (General Radio No. 759-B), the microphone of the meter being held in the position to be occupied by the head of the animal.

Exposures at 500, 1,000, 2,000, 4,000 and 7,000 cycles were also made with the Harvard Medical School system. The actual intensities obtainable with this system are not readily subject to direct measurement, but the intensity level can

Fig. 1. Organ of Corti of guinea pig x 360. Normal organ of Corti. Note mesothelial cells lying under the basilar membrane.

be estimated by comparing the damage obtained with that produced by the 598-B at the same frequency and known intensity.

After exposure, each ear was tested by measuring the threshold of the aural microphonics at 37 frequencies between 62.5 and 10,000 cycles. The difference between the threshold values of these animals and the average threshold values for the normal guinea pig is the "electrical" audiogram. All electrical tests were made just before the cochleas were fixed in Heidenhain's Susa solution.

All ears were cut in serial section and all sections were mounted and studied. Lesions found were indicated on a map of the cochlea. The map of the cochlea used is the same as the one previously reported in "The Localization of Pitch Perception on the Basilar Membrane."[1]

The damage produced by exposure to pure tones is confined to the cochlea. No evidence of vestibular damage to the utricle or saccule has been found. The middle ear mechanism gave no evidence of any traumatic changes due to the intense sounds used.

The minimum lesion that can be demonstrated, though subject to individual interpretation, is shown by changes

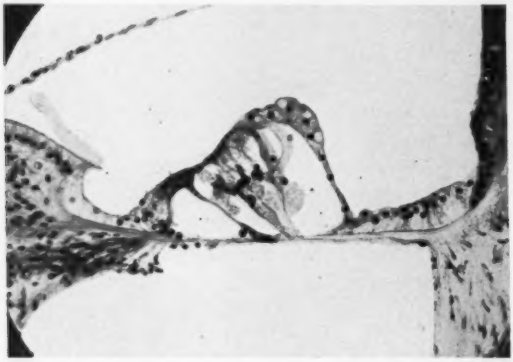


Fig. 2. Organ of Corti of guinea pig x 360. Organ of Corti essentially normal. Mesothelial cells stripped off the under-surface of the basilar membrane.

occurring in the protoplasm of the external hair cells. As these observations are so indefinite and, in all probability, subject to controversy, they have not been plotted except as questionable changes.

The smallest unquestioned damage is the stripping of the mesothelial cells lying under the basilar membrane. This lesion can be present without any other evidence of damage to the organ of Corti. In all animals having this minimum lesion, that were allowed to live for a number of days after their exposure, there was no regeneration of these cells (see Fig. 2).

The external hair cells are the next to be involved and they show degeneration or definite degenerative changes. The internal hair cells may or may not be involved in this process, depending chiefly on the length of time elapsing after the animal's exposure to sound. With increase of inten-

sity or increased time of exposure to the sound source, evidence appears of a separation of the organ of Corti from the basilar membrane or a break in the continuity of the organ of Corti, generally starting between the cells of Claudius and Hensen. The external hair cells and Deiters' cells may be lifted or thrown off the basilar membrane. This may be done with such severity that the external hair cells, with the supporting structures, detach themselves from the internal pillar

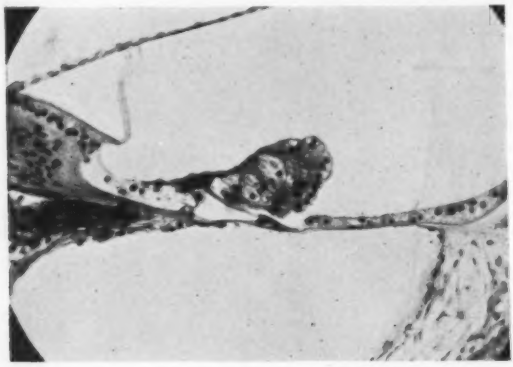


Fig. 3. Organ of Corti of guinea pig x 360. External hair cells and Hensen's cells lifted off the basilar membrane. Mesothelial cells absent under the basilar membrane.

cell, leaving only the cells of Claudius, the internal pillar cell and internal hair cells in their normal positions (see Fig. 3).

When there is a break in the continuity of the reticular membrane, it occurs over the external hair cells. The external hair cells and Deiters' cells then seem to ooze out through this break so that what remain are the internal hair cells, pillar cells, some of the Hensen cells and Claudius' cells.

The severest damage noticed was the complete disappearance of the organ of Corti. This may involve all structures between the internal sulcus cells and Claudius' cells; or there may be left resting on the lamina osseous spiralis the internal pillar cells and the internal hair cell. When this occurs there are definite degenerative changes of the internal hair cells (see Fig. 4).

If the animals are allowed to live for a number of days after exposure, degeneration of the organ of Corti continues

and may extend throughout the cochlea. To simplify the description of involvement of the organ of Corti, the lesions were classified into seven types in descending order of severity.

Type I: Organ of Corti thrown off basilar membrane. Degeneration of hair cells throughout the cochlea.

Type II: Organ of Corti thrown off basilar membrane. Degeneration of hair cells throughout the second and third turns and extending into the first and fourth turns.

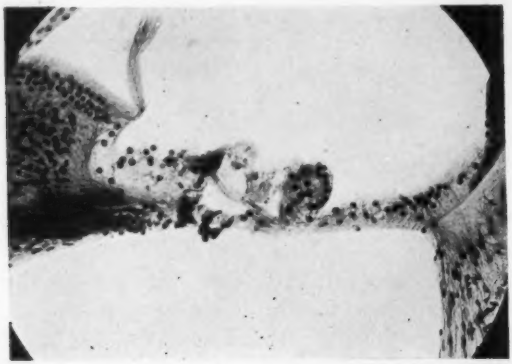


Fig. 4. Organ of Corti of guinea pig x 360. Rupture of reticular membrane with oozing out of the external hair cells. Hensen's cells are in normal relationship to the basilar membrane and the cells of Claudius. Mesothelial cells are absent under the basilar membrane. Degenerative changes in the internal hair cell.

Type III: Rupture of organ of Corti with degeneration of hair cells limited to the second and third turns.

Type IV: Some degeneration of hair cells but no rupture of organ of Corti.

Type V: Changes in cytoplasm of hair cells without definite changes, with or without loss of mesothelial cells.

Type VI: No changes in hair cells but some loss of mesothelial cells.

Type VII: No observable lesions.

The damage to the organ of Corti is in direct relationship to the intensity and duration of the tone used. In exposures with the 598-B to 500 cycles for three minutes at intensities from 141 to 153 dcb., minimum or no damage was found in

the organ of Corti from 141 dcb. up to 145 dcb. From 146 dcb. to 148 dcb., less than half the animals showed rupture of the organ of Corti. With intensities greater than 148 dcb. for three minutes, the lesions were of the maximum type.

The effect of increasing the duration of an exposure to 500 cycles at 150 dcb. was demonstrated by the increases in severity of the lesion with increase of time. Exposure of half a minute gave a damage of Type V. Exposure one to three minutes gave Types II and III. Exposures of four minutes and eight minutes gave Type I damage, the maximum effect. At 157 dcb., three seconds of exposure were not enough to rupture the organ of Corti, but 10- to 20-second exposures regularly produced lesions of Type II with rupture of the organ of Corti and widespread degeneration of cells.

The 598-B was also used for exposures at 1,000 and 2,000 cycles, but the intensities available at these frequencies were not sufficient to produce lesions of the more severe types. Of the series of ears exposed to 1,000 cycles at 148 dcb. for half a minute, three showed lesions of Type III with restricted rupture of the organ of Corti, two showed lesions of Type V, seven showed lesions of Type VI and two showed no lesions, Type VII. Of 10 ears exposed to 1,000 cycles at 140 to 141 dcb. for three to 10 minutes, none showed lesions more severe than the loss of mesothelial cells (Type VI). Exposures of 2,000 cycles showed that this frequency produced rupture of the organ of Corti in six ears exposed at 140 dcb. for 1.5 to six minutes. Intensities less than 140 dcb. produced lesions of Type V with simple changes in the external hair cells.

Exposures made with the Harvard Medical School sound system demonstrated that frequencies of 1,000, 2,000 and 4,000 cycles can produce lesions comparable with those made by the 598-B at 500 cycles, intensity 147 to 152 dcb. In cases where the bulla was opened before exposure the destruction of the organ of Corti was more complete than when the bulla was closed. The closed bulla seems to give a protection of five to 10 dcb. On comparing the lesions produced by the 598-B 2,000 cycles tone at 140 dcb. and that of the Harvard Medical School sound system at maximum intensity at 2,000 cycles for a similar length of time, the damage found indicated that the intensity of the Harvard Medical School sys-

tem cannot be less than 140 dcb. and may approach 150 dcb. The maximum intensities of the Harvard Medical School system for 500, 1,000 and 4,000 cycles must be greater than 140 dcb.

The location of maximum damage within the cochlea is found to be related to the frequency of the exposure tone. The loss of mesothelial cells is an excellent indication of the

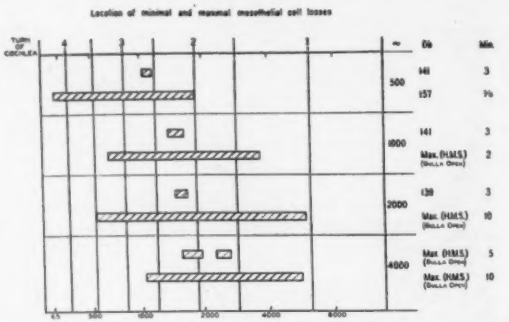


Fig. 5. Location of minimal and maximal mesothelial cell losses of the membranous cochlea in exposures to tones of 500, 1,000, 2,000 and 4,000 cycles at various intensities and time duration.

area in which the basilar membrane has been thrown into maximal vibration. The more intense the exposure tone the wider the region of mesothelial loss. The higher the frequency of the tone the closer to the round window is the region of the loss. With the 500 cycle exposure the minimum lesion of mesothelial cells was in the upper half of the second turn or the lower half of the third turn. The maximum lesion for the 500 cycles was from the junction of the first and second turns to the upper half of the fourth turn. For 1,000 cycles the minimum lesion was in the upper half of the second turn. The maximal lesion was in the upper half of the first turn to the upper half of the third turn. At 2,000 cycles the minimum loss was in the upper or lower half of the second turn and the maximum loss was from the middle of the first turn to the junction of the third and fourth turns. Exposure to 4,000 cycles gave a minimum loss in the lower half of the second turn, and maximum lesion from the middle of the first turn to the junction of the second and third turns.

Exposures at 7,000 cycles did not throw off the mesothelial cells though there were changes or degeneration in the hair cells of the first and second turns. The maximum intensity of this tone obtainable by our apparatus was evidently insufficent to cause a loss of mesothelial cells.

The region of maximum damage to the organ of Corti was usually close to the center of the region from which mesothelial cells were missing, and, therefore, bears a similar

Fig. 6. Organ of Corti of guinea pig x 360. Seven days after exposure to the traumatic tone. Generalized degeneration of the organ of Corti. Mesothelial cells are absent.

relation to the frequency of the exposure tone. The evidence we have at present indicates that the centers of maximum vibration for the four frequencies tested (500, 1,000, 2,000, 4,000 cycles) are more closely spaced within the second and third turns than is suggested by the map of the cochlea used by Stevens, Davis and Lurie (see Fig. 5).

Traumatic changes in the membranous cochlea which can be detected by histological methods are apparently permanent. We have observed no indication of regeneration of the organ of Corti or of the mesothelial cells during periods as long as 55 days after exposure. Progressive degenerative changes have been observed in the organ of Corti until it has been replaced by a single layer of epithelial cells. The nature of this absorption, which may start within two days after the exposure, is still obscure. This process of degeneration and absorption has been previously reported.[2] The

degeneration of the nerve fibres and the cells of the spiral ganglion starts at a later time. Fibre degeneration has been observed as early as nine days after the exposure but degeneration of the ganglion cells starts at a much later time, probably from three to four weeks after exposure. The degeneration of the nerve fibres and spiral ganglion cells appears first in the region of maximum damage, where there is no organ of Corti (see Figs. 6 and 7).

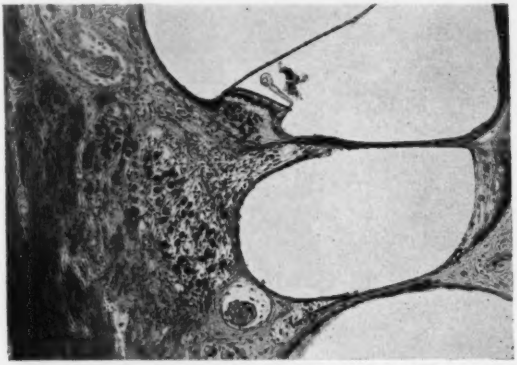


Fig. 7. Third turn of the cochlea of guinea pig x 200. Fifty-five days after exposure to a traumatic tone. Complete disappearance of the organ of Corti. Mesothelial cells are absent. Degeneration of the cochlear nerve fibres and of the spiral ganglion.

The elevation of the threshold of the aural microphonic after exposure is related to the degree of anatomical damage produced by the exposure tone, which in turn depends upon the frequency, intensity and duration of the tones. The loss of sensitivity, however, is seldom restricted to a narrow band of frequencies. It is clearly related to the degree of anatomical damage, although losses exhibited by ears which have sustained similar lesions are not necessarily equal. When the loss is relatively slight, the lower frequencies are usually more affected than the higher frequencies. With more severe lesions the loss is greater at higher frequencies and may be complete. The loss produced by exposures to 2,000 cycles at 140 dcb., associated with moderate lesions of types III, IV and V, is usually greater at the middle frequencies (500 to 4,000 cycles). Exposure to the maximum intensity of the Harvard Medical School sound system at 2,000 and 4,000 cycles caused severe losses which were greatest for the high tones and least for the lower frequencies.

These losses when plotted as an audiogram as a rule gave a curve without sharp breaks. Such an audiogram is shown in Fig. 8, with the chart showing the lesion (type II). The ear was tested two days after exposure to 500 cycles at 150 dcb. for two minutes. Absorption of the organ of Corti had already begun in the second and third turns. Considerable loss is apparent throughout the region of degeneration, but there is no dip corresponding to the area in which the organ of Corti is missing. The loss is least for frequencies above

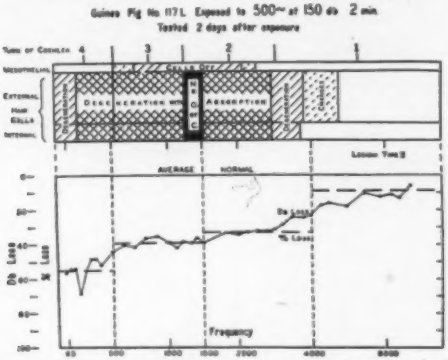


Fig. 8. Map of lesions found in the cochlea and electroaudiogram of a guinea pig exposed to a 500 cycle tone at an intensity of 150 dcb. for two minutes. Ear tested two days after exposure.

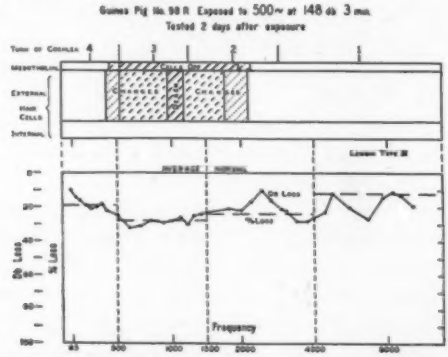


Fig. 9. Map of lesions found in cochlea and electroaudiogram of guinea pig exposed to 500 cycles at 148 dcb. for three minutes. Tested two days after exposure.

4,000 corresponding to the uninjured lower half of the first turn. A less severe lesion of type IV with its audiogram is shown in Fig. 9. The lesion and audiogram of an ear exposed

to 4,000 cycles at maximum intensity of the Harvard Medical School sound system for 10 minutes is shown in Fig. 10. Here, there is some loss of sensitivity throughout the frequency range, but the loss increases rapidly above 1,000 cycles; that is, in the boundary region between "degenerative changes" and complete degeneration. This type of break in the audiogram has been found in ears tested within an hour after exposure, and only rarely in ears tested several days after exposure. One can only conclude that the progressive

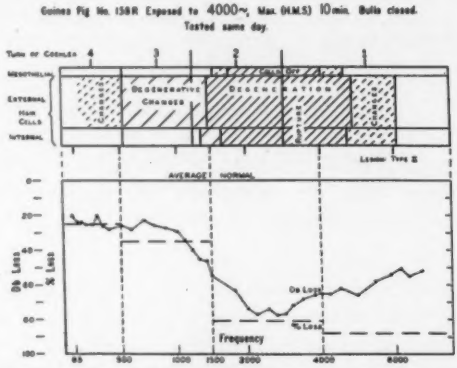


Fig. 10. Map of lesions found in the cochlea and electroaudiogram of a guinea pig exposed to 4,000 cycles maximum intensity of the Harvard Medical School sound system for 10 minutes. Tested immediately after exposure.

changes occurring over a period of days tend to decrease the response at frequencies which were only slightly affected immediately after exposure.

With the present data we can only say that it is still impossible to determine the exact correlation between pathological changes of the organ of Corti and the loss of sensitivity of the aural microphonics.

SUMMARY.

Guinea pigs were exposed to pure tones of various frequencies at intensities from 140 to 157 dcb. The least detectable anatomical damage to the organ of Corti was disappearance of the mesothelial cells in a limited area from the scala tympani surface of the basilar membrane. This was produced by 1,000 cycles at 140 dcb. for three minutes. Severe

and extensive damage is produced by more intense tones and by longer exposures. The damages produced by intense tones are degenerative changes, rupture and dislocation of the organ of Corti from the basilar membrane. A few days or weeks after exposure, the organ of Corti disappears where it had been severely damaged, and the nerve fibres and ganglion cells begin to degenerate.

Mild degrees of damage are localized, but a severe exposure (150 dcb. for several minutes) causes widespread damage. The damage tends to locate nearer the helicotrema when caused by low tones and nearer the round window when caused by high tones.

Once the organ of Corti has been damaged and degeneration of cells is present, there is no regeneration of the cells. The final result of these lesions is complete absorption of the damaged cells with an accompanying degeneration of the nerve fibres and ganglion cells leading from the site of the lesion.

Severe and extensive damage can be caused to the organ of Corti by loud tones without apparent injury to the eardrum or ossicles.

The electrical activity of the cochlea (Wever and Bray effect or aural microphonics) is impaired by exposures which cause definite anatomical changes in the organ of Corti. There is some general correspondence between changes in the "electrical audiogram" and the anatomical changes, but the parallelism is not exact or invariable. The study of the anatomical changes is a more consistent and a more reliable method of estimating injury to the organ of Corti than the electrical activity of the cochlea.

BIBLIOGRAPHY.

1. Stevens, S. S.; Davis, H., and Lurie, M. H.: The Localization of Pitch Perception on the Basilar Membrane. *Jour. Gen. Psychol.*, 13:297-315, 1935.

2. Lurie, M. H.: The Degeneration and Absorption of the Organ of Corti in Animals. *Ann. Otol., Rhinol. and Laryngol.*, 51:3:712, Sept., 1942.

THE PROGRESS OF AVIATION OTOLOGY IN WORLD WAR II.*†

LIEUT. COL. PAUL A. CAMPBELL,
M.C., U.S.A.

When the spreading European and Asiatic conflagration showed evidence of attacking the shores of America, a nucleus of far-seeing men, centered about Lieut. Colonel David N. W. Grant, now Major General Grant, the Air Surgeon, was laying plans for the possible expansion of the medical services for the Air Forces. Theirs was the tremendous problem of formulating plans by which tens of thousands and if need be hundreds of thousands of young men could be selected, then classified as pilot, navigator, bombardier, air-crewman or ground service man, and finally cared for during their preparation for the possible defense of their homeland.

It was the lot of a few of us to be ordered into service in the initial stage of this preparation. It is my fortune to have had an assignment which made it possible for me to observe a period in which there was reshuffling and change in emphasis of various of the aspects of Aviation Otology. Today, in generalities, and I emphasize the term generalities, I will report some of these developments.

To be sure, the roots of Aviation Otology previously had been firmly embedded in rich soil. Many of the members of this organization had their share in the planting of these seeds and had nurtured the seedlings well through the era of their early growth. Your roster includes the names of many otologists whose names will live wherever men may fly, be it in peace or in war.

It would be a presumption on my part to attempt to tell this organization anything of Aviation Otology during that early period. In general, selection standards had been proven

*Read at the Seventy-seventh Annual Meeting of the American Otological Society, Inc., New York, June 5, 1944.

†From the Research Laboratory of the Army Air Forces School of Aviation Medicine, Randolph Field, Tex.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, July 12, 1944.

adequate, care of the ears of the flyer had been placed upon a firm foundation, and the otological elements of blind flight had to a great degree been perfected.

As more and more evidence began to present itself that our shores might not remain untouched in a world of flame, plans for expansion of the Air Force medical service began to take shape. The mission of those of us who were otologists was projected as follows: First, to train a sufficient number of physicians to handle the otological situations which might arise; second, to prepare to alter selection standards if such became necessary for maintaining an adequate flow of Air Force personnel to meet an expanding program; and third, to institute an investigation media through which the personnel of the Air Forces could receive all possible protection from the otological viewpoint, and could also receive the benefits of any new otological or acoustical engineering developments which might aid them in the performance of their duties.

The plans, of course, had to be premised on certain conditions which had not been presented in the earlier phase of Aviation Medicine. First of all, whereas a few thousand people had been flying, hundreds of thousands might be required to fly. Aircraft had grown larger, and their crews had increased in size. Planes had become faster, more powerful and operational altitudes had more than doubled. Last but not least, the operation of flying personnel might be worldwide in scope.

THE TRAINING OF AVIATION OTOLOGISTS.

The preparation of the general run of the mill physician to care for the otological conditions with which he might be confronted took no little consideration, as most of the physicians were general practitioners or specialists in other fields.

Early in 1940, training of medical officers to become Flight Surgeons was accelerated. Whereas the first class of that year graduated eight, in the last class of the year there were 40. The class graduating just before the Pearl Harbor attack consisted of 86 members. One of the members of that class was the first medical officer to lose his life in World War II.

He was Lieut. William R. Schick, Medical Corps, who was shot down as he and his unsuspecting companions flew into Pearl Harbor on that eventful morning. After Pearl Harbor large numbers of physicians were assigned to the Air Forces as medical officers.

To teach these medical officers, who for the most part had just left civilian practice, to recognize ear diseases, make hearing tests, understand the mechanism of the vestibular apparatus, along with the various other phases of Aviation Medicine, was no small task. These embryonic Flight Surgeons had to be trained in all of the aspects of air medicine, and among other things taught to build slit trenches, construct bomb shelters, prevent malaria, care for camp sanitation, and numerous other duties peculiar, in their lives at least, to war. Thus their course in otology was short but concentrated; however, subsequent reports from the field have indicated that these men are equally adept in all phases of their work.

ALTERATION OF OTOLOGICAL STANDARDS FOR FLYING PERSONNEL.

As has been stated, the otological standards as devised during and after World War I had been proven for the most part adequate. Early in the combat phase of World War II the question arose, "Could these standards be revised downward if a shortage of material from which selection could be made became evident?" To date an answer has not been necessary. Otologically speaking, the proverbial bottom of the barrel, the anticipation of which caused no little concern in the early stages of the war, has not been sighted and there is no reason to believe it will even be approached. The various selection procedures, otological and otherwise, have to a slight extent been altered from time to time, but these changes have been largely to improve technique rather than to lower qualification standards. All tests have been kept under statistical surveillance in order that the elimination rate of any single or group of procedures could be watched in perspective. Also, much investigative work has been carried out for the purpose of validating the various procedures, using as criteria successful completion of flying training and wherever possible performance in combat.

RESEARCH IN AVIATION OTOLOGY.

To date much research effort has been spent relative to the problems of aviation otology. The work has been performed for the most part through the co-ordinated activity of civilian and military agencies. For your interest a few of the more pertinent aspects of these problems and the results of some of the investigations will now be considered.

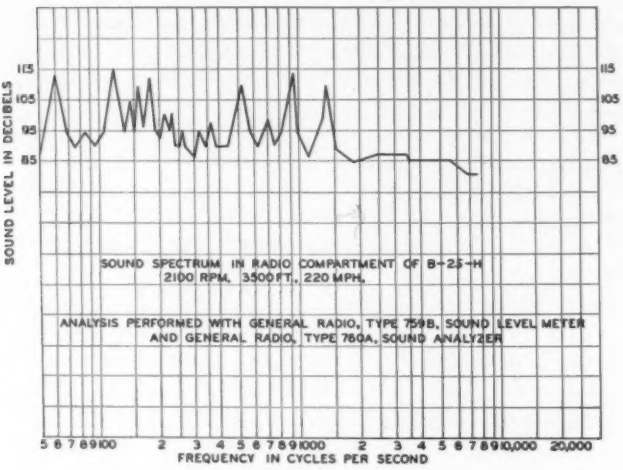

SOUND LEVEL IN DECIBELS
115
105
95
85
SOUND SPECTRUM IN RADIO COMPARTMENT OF B-25-H
2100 RPM, 3500 FT., 220 MPH.
ANALYSIS PERFORMED WITH GENERAL RADIO, TYPE 759B, SOUND LEVEL METER
AND GENERAL RADIO, TYPE 760A, SOUND ANALYZER
5 6 7 8 9 100 2 3 4 5 6 7 8 9 1000 2 3 4 5 6 7 8 9 10,000 20,000
FREQUENCY IN CYCLES PER SECOND

Fig. 1.

THE EFFECT OF AIRCRAFT NOISE UPON THE EAR.

Just as the magnitude of the numbers of men, the expense, the casualties and the geographical scope of war have increased century by century, so has the din of war increased. Whereas in peacetime the noise to which one is subjected while flying in aircraft is largely limited to that produced by the engine, propeller and slipstream, in war the intense noise of machine gun and automatic cannon fire is added along with that of bursting bombs, flak and ground explosions. An example of the noise spectrum of an aircraft in flight is shown in Fig. 1.

In this particular aircraft, as can be seen, the noise intensity under 150 double vibrations per second reaches 115 dcb. It then slopes off and at a frequency of 2,000 d.v. it reaches

a level of 85 to 90 dcb. The final effect of this trauma to the acoustic mechanism of service personnel cannot be evaluated for some time. Groups are suveying the rehabilitation centers and redistribution centers for evidence which might point to trends; however, it probably can be safely said at this time that the problem of aural casualties has not even approximated that which was expected.

It is a matter of common knowledge that sustained white noise at high intensity affects hearing. By the term white noise is meant noise of all frequencies mixed together just as white light is a mixture of all frequencies.[1] The effects of this noise are both acute and chronic.[2] The acute effects are usually manifested by a notching of the audiogram at a frequency in the neighborhood of 4,000 d.v. This notching is in most instances reversible and fits into the usual conception of fatigue in that there is a relationship between the magnitude of the fatiguing noise and the intensity of the hearing loss produced. Likewise, there is a relationship between the time the fatiguing force is applied and the time of recovery. The chronic effects consist of a permanent notching and a fan-wise spreading of the notch. The character of this notch is identical with that which is noted in the acute form, but it is not reversible.

It is fortunate that the notching of an individual's hearing curve is usually above the frequency of the conversational range and the range for the usual musical tones. Thus subjective complaints of hearing loss have to date been uncommon; in fact, it is not unusual in routine audiometric studies of flyers who have had many hours in the air to find those with rather large hearing defects above 3,000 d.v. but who still hear a whisper at 20 feet.

It is also quite evident that there is a great variation among individuals as to vulnerability to both the acute and chronic effect of noise. Whereas a white noise of 110 dcb. will cause acute hearing changes in one individual after a duration of one hour, in another individual four hours of the same trauma will not cause a perceptible change. The same phenomenon is manifest in the chronic irreversible changes. There is in my possession the audiogram of a youngster who has perma-

nent notching after 200 hours of flight. On the other hand, I have the audiogram of a pilot with 20,000 hours of flight showing no effect whatsoever.

What is the reason for the vulnerability of this tone area and why is there such widespread individual variation? Crowe, Polvogt[3] and other investigators have pointed out that the upper tone ranges are affected by many processes such as Eustachian tube obstruction, toxins, both endogenous and exogenous, and trauma of various sorts. It has also been stated that there is an anatomical basis for the manifest vulnerability in that the blood supply of the basal turn of the cochlea — the affected representation area — is deficient; further, that that area is most exposed to the various forms of trauma which are transmitted either by air conduction or by bone conduction. Bekesy[4] and others have pointed out that the natural resonance of the external auditory canal is such that all tones entering the canal are intensified in the 3,000 frequency range. Consequently, that area is continuously subjected to sounds more intense than those which reach other areas.

A possible suggestion occurs when one considers the audiometric studies which have been performed by Elder[5] and others upon chimpanzees. Their composite audiograms demonstrate that there is a natural elevation of the auditory threshold in these animals in the 4,000 region. Thus the adage that those functions last to appear in phylogenetic development are the least resistant to destructive processes can possibly be applied.

Concerning the increase in vulnerability demonstrated by certain individuals, little is known; however, it may be said that certain individuals are affected more than others by fatigue, toxins, etc. Thus it would seem reasonable that individuals would show widespread variation to the effects of noise.

As there is great individual variation in vulnerability to noise, much effort is being devoted toward the development of a test which will discriminate between those vulnerable and those who are not vulnerable. Some of the work is quite promising.

THE EFFECT OF NOISE UPON COMMUNICATIONS INTELLIGIBILITY.

From the standpoint of the problem of aviation, noise has another important detrimental effect: its interference with communications intelligibility. Airmen depend upon radio communication for take-off and landing instructions. Weather information, combat orders and changes in flight plan must come to them by auditory perception. In flight, confusion of such simple words as "northeast" and "northwest" might lead to serious consequences. Furthermore, a 1,000 cycle beam is the pilot's roadway of the air along which he must fly by auditory perception. The crossings of the beams are the mileposts upon which he must rely for the determination of his exact position, ground speed, fuel consumption, wind drift and for other information important to the successful and safe completion of his mission.

Lately, it has become quite evident to otologists and psychologists that certain manifestly normal individuals hear better in noisy surroundings than do others. Again, it is important from the standpoint of selection to determine just who these men are. Consequently, tests directed toward that goal are in the process of development.

It should also be noted here that pure tone audiometry will not afford all the information necessary in the critical selection of the men who are best able to meet communications requirements efficiently. The correlation between pure tone audiometry and word test audiometry is not high. Consequently, it is my belief that from this war will come a mass audiometric test which will contain the various elements necessary for aircraft communication and operation. That is, a combination of the pure tones of the beams and the dots and dashes of Morse code signals along with selected spoken words all in a background of noise. Several such tests are in the process of development.

PROTECTION AGAINST NOISE.

Protection against aircraft noise can be applied either to the aircraft or to the ears of the airman. Neither have been eminently successful as far as military operation is concerned. Noise, to a great extent, is an inescapable resultant of power and speed, both of which are military necessities. Elimination

of the noise producing factors eliminates the function of the aircraft. The engines can be stopped and the propellers feathered but until the aircraft ceases to move through the air mixed noises of high intensity are present. The noise of gliders moving through the air without benefit of power plant or propellers has at times been recorded as high as 110 dcb. in certain frequencies.

Again, militarily speaking, soundproofing has failed to produce desirable results. Soundproofing for the most part is a function of the weight and bulk of the material applied as well as the ability of the engineer to tightly seal the aircraft from outside sound sources. To a great degree, all must be dispensed with in combat aircraft as each additional pound must by that amount decrease gasoline and bomb load or affect rate of climb, maneuverability and ceiling. Each cubic foot of bulk decreases carrying space and streamlining. Tight seals for the most part are not feasible as guns must protrude and swing through wide arcs.

Direct protection of the ears has involved the development of sound isolating helmets and communication headsets. Ear defenders which fit directly into the external auditory canal are now being produced by various manufacturers and laboratories. None, however, as yet meets all of the requirements of the perfect defender. Efficient masking of ambient noise while permitting conversation and signals to pass are necessary attributes for an acceptable defender. It must at the same time be simple to apply, comfortable, and nonirritating, cleansable and capable of equalizing changes in barometric pressure coincident with altitudinal change. Twisted cotton, with or without a lubricant, has long been the favorite protective device of those who fly, because it is easily procurable, can be fashioned to fit any ear canal, and can be worn beneath headphones. It may also be thrown away after it is used. While its masking characteristics do not compare favorably with some of the new defenders, it will, in my opinion, remain the personal choice of airmen until a defender is offered to them which equals the simplicity of application and presents better masking characteristics.

Research Pertaining to Aero-Otitis Media has continued throughout the war, as it has presented a problem from the standpoint of lost flying hours. The highest incidence has

occurred during or after simulated flights in pressure chambers or during episodes of upper respiratory infections. As you are no doubt aware, one of the outstanding achievements of this war has been the use of pressure chambers for the indoctrination and classification of flying personnel. Early in flying training the aviation student makes a pressure chamber flight to 35,000 feet under the careful scrutiny of a specially qualified Aviation Physiologist who, while studying him from the standpoint of his physical reactions to simulated altitude, indoctrinates him in his need for and in the use of oxygen. In spite of a preliminary short flight to about 8,000 feet for the purpose of eliminating those who have blocked Eustachian tubes and have not been eliminated by previous examination, a certain number of aero-otitis media cases develop. These individuals are then given further study and, if necessary, remedial measures are instituted. In by far the larger number of instances a little training in the proper use of the Valsalva maneuver or further admonition not to undergo barometric pressure change while experiencing a head cold suffices. Thus in most instances aero-otitis media, militarily speaking, is a problem of selection and training.

External Otitis, on the other hand, has proven itself a problem in hot, humid combat areas which have been occupied as a result of the global scope of the war. Outstanding contribution in the treatment of those cases due to fungi has been made by Captain Ben Senturia and Corporal Fred T. Wolf,[6] of the Research Laboratory of the School of Aviation Medicine, in their study of the fungistatic effect of powdered sulfanilamide on Aspergillus, Penicillium and Mucor.

RESEARCH IN AIRSICKNESS.

It would probably be remiss to close this discussion without a word concerning the vast amount of study by the British, the Canadians, the Russians and ourselves which has been directed toward the study of airsickness. Again, this problem has been approached from two angles: First, the angle of selection; second, the angle of therapy.

Early in this study it was realized that the correlation between abnormal vestibular reactions as measured by the Bárány chair tests and airsickness was not high, thus that

variables existed which had to be ascertained before selection of those susceptible to airsickness could be adequately accomplished. With this in view, various synthetic motion producing devices were designed and studied. Most of the group studying the problem in the early phases of the work agreed that a swing with a radius of about 14 feet had a higher correlation with airsickness than other devices tried. It was realized, however, that the correlation was by no means perfect; thus, to use only such a device for selection would prove costly as it would eliminate certain men who might be good flyers and miss others who undoubtedly should be eliminated. A search for other variables then led to the belief that, as had long been suspected, in certain individuals there was a strong psychogenic element. Consequently, in our group at least, the following conception of airsickness has been agreed upon.

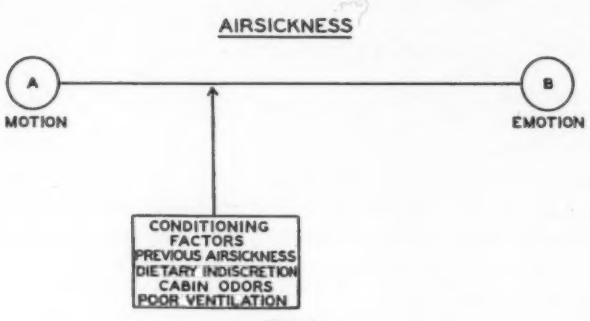


Fig. 2.

As is shown in the diagram, airsickness in a given individual may be due to motion or emotion. By emotion is meant any psychogenic reaction associated with flight, the most severe of which is fear of flight. Airsickness can be produced by motion alone or by emotion alone, but as is most often the case, a mixture of the two elements is present. Thus, any airsick individual is considered to be represented by some position along the line A-B. This position may vary from time to time, or in other words, the individual may be conditioned by previous airsickness, dietary indiscretion, fatigue, cabin odors, poor ventilation and other factors; however, this variation is not great. Many of those in whom the motion

factor is predominant have been found able to adapt themselves to the motion of aircraft after a certain length of time. Few of those in whom the emotion factor is predominant have been found who progress well in the flying training program.

While careful history of past reaction to motion, the use of a carefully evaluated psychoneurotic study by interview as performed in the study known as Adaptability Rating for Military Aeronautics and a swing test will give one a workable selection procedure, it remains true that several actual flights under varying conditions is as yet the only highly reliable selection procedure.

Much investigation of the problem of therapy is being carried on. Hyoscine and hyoscine-like drugs are among the most efficient protectors found to date; however, any drug used in flying personnel must be prescribed with extreme care.

In closing, it must be stated that the material which has been reported today has been the result of the co-operation of many individuals of the United Nations, both military and civilian. Much excellent work will probably go unreported in detail until the war is over. Obviously, time has not permitted the mention of the names of the many, many investigators who have played such an important part in the progress of Aviation Otology in World War II.

REFERENCES.

1. Carson, L. D.; Miles, W. R., and Stevens, S. S.: Vision, Hearing and Aeronautical Design. *Federation Proc.*, 2:2:126-129, June, 1943.

2. Campbell, P. A.: Aviation Deafness — Acute and Chronic. *Arch. Oto.*, 32:417-428, Sept., 1940.

3. Crowe, S. J.; Guild, S. R., and Polvogt, L. M.: Pathology of High Tone Deafness. *Bull. Johns Hopkins Hosp.*, 54:315-379, 1934.

4. Bekesy, G. v.: Uber den Einfluss der durch den Kopf und den Gehorgang bewirkten Schallfeldverzerrungen auf die Horschwelle. *Ann. d. Physik.*, 14:51-56, 1932.

5. Elder, J. H.: Auditory Acuity of the Chimpanzee. *Jour. Comparative Psychol.*, 17:2, April, 1934.

6. Senturia, B. H.; Treatment of External Otitis — Local Sulfanilamide Therapy. Part I. Unpublished.

————, and Wolf, F. T.: Treatment of External Otitis — Local Sulfonamide Therapy. Part II. To be published.

THE TREATMENT OF EPISTAXIS BY SCLEROSING INJECTIONS.*

SAMUEL L. FOX, M.D.,

Baltimore.

While working with sclerosing solutions during the past few years to reduce the size of the turbinates in chronic vasomotor rhinitis,[1] the author became interested in the possibilities of treating bleeding vessels in the nose by sclerosing injections. At first the technique was attempted on small anterior septal varicosities that were the cause of recurrent epistaxis. The results in this series of cases were uniformly satisfactory. The varicosities were obliterated in every case, usually by one injection of the sclerosing agent; only seldom was a second injection necessary.

In the beginning, if the case was seen during active bleeding, an actual cautery or some chemical coagulant was first applied to control the immediate hemorrhage. The sclerosing agent was injected several days later to prevent a recurrence. Cauterization of any actively bleeding vessel is a most difficult procedure, since the coagulant, whether chemical or heat, usually expends itself upon the blood which has been ejected from the broken vessel, and soon the cautery or chemical application is worthless until cleaned or renewed. Because of this, the author conceived the idea of injection of the sclerosing solution beneath the bleeding point during the active phase of bleeding, expecting that the distention of the mucosa by the sclerosing solution would produce enough pressure to control the hemorrhage. In practice this procedure has proven easy of operation and very successful. At present, therefore, the author has dispensed with the cautery and simply injects the sclerosing solution in the presence of active bleeding, thus achieving a dual effect: immediate control of the bleeding, and permanent obliteration of the vessels by sclerosis.

---

*From the Department of Otolaryngology of the University of Maryland School of Medicine.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, July 31, 1944.

TECHNIQUE.

In actively bleeding cases, a pledget of cotton moistened with either 0.5 per cent pontocaine solution or 4 per cent cocaine hydrochloride solution is applied firmly against the area for several minutes. This provides adequate anesthesia for the subsequent injection and frequently provides a temporary measure of control for the bleeding. The cotton tampon is quickly withdrawn from the nose and from 0.25 to 0.5 cc. of Sylnasol* (sodium psylliate solution, Searle) is injected *into* the mucosa just beneath the bleeding point, so that a vesicle appears, using a tuberculin syringe and hypodermic needle. The vesicle thus raised almost always controls the active bleeding by the pressure resulting from the distention of the tissues. If the bleeding is thus controlled, nothing further is done; otherwise, another 0.25 cc. of Sylnasol is injected similarly after a few minutes. In no case has more than two injections been necessary. Should this fail, however, actual pressure packing would be required for the immediate control of the bleeding. This could then safely be removed in 24 hours as the effect of the sclerosing agent would be present. Following such an injection, the patient is observed every other day for the next week, by which time the bleeding vessel has become completely obliterated by sclerosis. If any other varicosities exist, a similar injection is performed again at the end of a week's time.

If the patient presents himself with septal varicosities which are not bleeding at the time, the author injects 0.25 cc. of Sylnasol intramucosally at the site of the vessels under pontocaine anesthesia. One such injection will obliterate a number of small vessels, providing the solution is injected *intra*mucosally and not submucosally and providing the solution is made to diffuse across the entire area involved. This can be observed at the time of the injection by the blanching effect on the mucous membrane.

OBSERVATIONS AND RESULTS.

More than 100 patients, both children and adults, have been treated for recurrent or acute epistaxis by injecting a sclerosing solution into the mucosa at the site of the bleeding

*The author acknowledges the kindness of the G. D. Searle and Co., Chicago, in supplying the "Sylnasol" used in this investigation.

point. The results have been excellent. In every case where the bleeding point could be located, the hemorrhage has been controlled by this technique. In the chronic recurrent variety due to varicosities, occasionally several injections at weekly intervals have been necessary to obliterate all of the vessels. Usually, however, one injection suffices. Where varicosities exist on both sides of the septum, the author has preferred to inject one side at a time, repeating the procedure after three or four days on the opposite side. This prevents both sides of the nose from being partially obstructed at once due to the moderate edema which follows each injection.

To date the author has employed Sylnasol injections in the nose in more than 500 cases of chronic vasomotor rhinitis and in epistaxis; no serious side-effects have been observed and there have been no complications. The patient may experience a sense of fullness in the nose, slight retrobulbar discomfort, moderate lacrimation or some sneezing; but nothing more serious has been observed. The side-effects are quite transient and last only five or 10 minutes. The resultant edema at the site of the injection often produces slight nasal obstruction on that side for a few days. This is seldom severe enough to be annoying, however.

SUMMARY AND CONCLUSIONS.

1. More than 100 patients have been treated for recurrent or acute epistaxis due to septal varicosities by injections of a sclerosing agent (Sylnasol) intramucosally at the site of the bleeding point or varicosities.

2. The results have been uniformly satisfactory: active bleeding has been controlled immediately, and the vessels subsequently have become obliterated by sclerosis so that recurrence of the bleeding is obviated.

3. From 0.25 cc. to 0.5 cc. of Sylnasol are employed, and this is injected intramucosally (not submucosally). Injection into the vessels themselves has not been attempted nor is it advised, since the intramucosal injection is safer, has the immediate effect of controlling active hemorrhage and is equally efficient in the subsequent sclerosing process. In addition, all the vessels of a given area are affected by the injec-

tion when it is done intramucosally, whereas only one vessel would be affected if the vessel itself could be injected.

4. Usually one injection is adequate at each site for the control of bleeding or the obliteration of varicosities.

5. No complications and no serious side-effects have been observed.

BIBLIOGRAPHY.

1. Fox, S. L.: Chronic Vasomotor Rhinitis. A Clinical Investigation of Its Treatment with a Sclerosing Agent. THE LARYNGOSCOPE, 53:12:759, Dec., 1943.

1820 Eutaw Place.

UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE.

The University of Illinois College of Medicine announces that its fall didactic and clinical refresher course for specialists in otolaryngology will be held at the College from Sept. 25 to 30, inclusive. The fee for the course is $50.00. Since registration is limited to 25, applications should be filed as early as possible. Write for information to Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Ill.

THE USE OF A BRONCHOSCOPE TO MAINTAIN AN AIRWAY. REPORT OF A CASE.

RICHARD W. HANCKEL, JR., M.D.,

Charleston, S. C.

The following case is presented because of the interesting pathogenesis of the infection and the necessity of maintaining an airway by means of a bronchoscope after a tracheotomy cannula had proven inadequate.

M. S., a white female, 27 years of age, was admitted to Pinehaven Sanatorium, Charleston, S. C., on Jan. 31, 1940.

Her chief complaint was "wheezing in the chest." She stated the onset of her trouble was a sore throat which began about July 15, 1939. She subsequently developed a hoarseness, a low grade fever and a nonproductive cough. Being a student at the University, she was admitted to Duke Hospital at the time, on July 18, 1939, and remained there a week. She states that X-rays taken on admission showed a small amount of fluid in her right base. A second X-ray taken before her discharge a week later was reported normal. All of her systems cleared while she was in the hospital except for the nonproductive cough, which has persisted up to the present time. About the time of the onset of the cough she developed a wheezing in her chest. This has diminished since onset and is now audible only on exertion. She returned to Charleston in August, 1939, and has gained 10 pounds in weight and feels stronger.

She denied having hemoptysis, night sweats, chills or weight loss. There was no history of recent exposure to tuberculosis, but she stated that in 1935 she boarded in the same house with a man who was diagnosed as having tuberculosis three days before she moved from the house.

Physical examination revealed a well developed and nourished cooperative female, apparently of stated age.

Chest examination showed expansion equal on the two sides. There were increased breath sounds posteriorly on the right along the border of the scapula. Wheezing was noted in the posterior axillary line at the level of the seventh rib. Otherwise the physical examination was essentially negative.

X-ray of the chest, Jan. 15, 1940, showed accentuated bronchovascular markings in the right lower lobe suggesting the possibility of bronchiectasis.

Laboratory findings: Sedimentation index, Feb. 4, 1940, was 28.

Blood count on admission was as follows: Hgb., 12 GMC.; total white cells, 5,700; large lymphocytes, 21 per cent; small lymphocytes, 13 per cent; large monocytes, 4 per cent; neutrophiles, 58 per cent; eosinophiles, 4 per cent.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, July 31, 1944.

Sputum on admission was negative for tuberculosis, but became positive Feb. 10, 1940.

Progress: Artificial pneumothorax of the right lung was begun on Feb. 13, 1940, three days after the first positive sputum, and continued

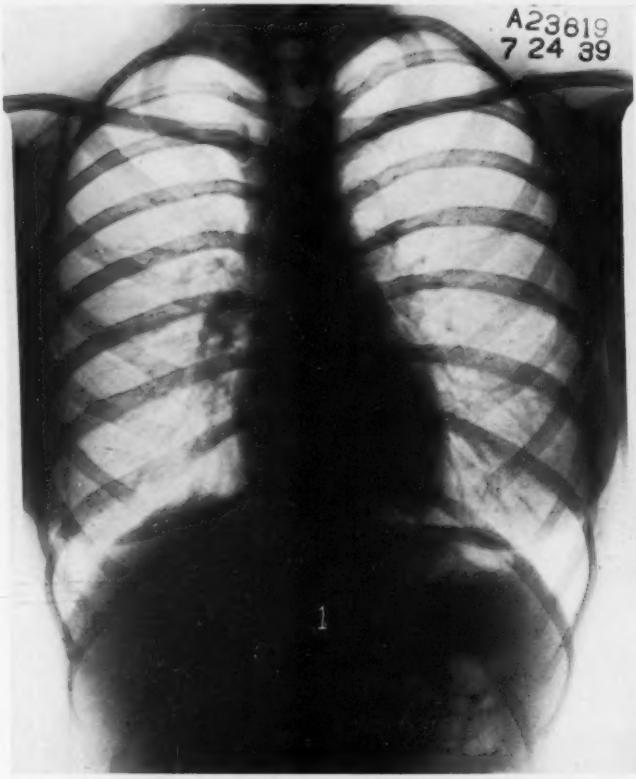


Fig. 1. X-ray taken at Duke, showing an apparently normal chest.

throughout her stay in the sanatorium. A good collapse was obtained. On May 6, 1940, 150 cc. of fluid were removed from the left side.

The sedimentation index gradually decreased from 28 on admission to 22 on Sept. 19, 1941.

Smears for tuberculosis were negative until Feb. 10, 1940, at which time a Gaffky I smear was reported. It again became negative (i.e., after pneumothorax was begun) until April 27, 1940, when a Gaffky IV smear was reported. The smears remained positive after that, the last reported being Jan. 15, 1941.

She was transferred to State Park, Columbia, S. C., March 9, 1941, for bronchoscopic examination. She returned March 29, 1941. The indications for bronchoscopy at this time were a continued positive sputum in spite of a good collapse of the right lung and rather frequent attacks of dyspnea. The report from State Park revealed extensive tracheobronchial tuberculosis with ulceration.

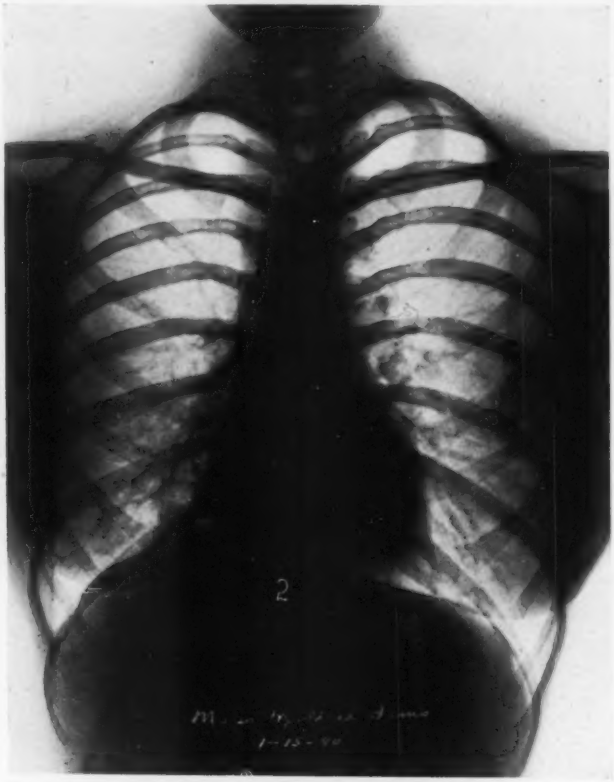


Fig. 2. Accentuation of the bronchovascular markings is noted on the right base, suggesting the possibility of bronchiectasis.

The patient got along fairly well except for occasional attacks of dyspnea and wheezing and coughing following this. Her symptoms were relieved by steam inhalations and bed rest with occasional hypodermic injections of adrenalin M.ii to iv.

On Sept. 14, 1941, she had another attack of dyspnea and following this she was able to breathe comfortably only when lying on her left side. She would become dyspneic whenever she would lie on her right side or back. She remained in bed all the time and used steam inhalations constantly.

On Nov. 10, 1941, progress note states "patient had a severe attack of dyspnea lasting an hour. She was somewhat relieved on expectorating some mucus. She was moved to a private room. The dyspnea is severe and progress poor."

The patient was first seen by the author in consultation with Dr. W. A. Smith on Nov. 13, 1941. Steam inhalations were advised continued and

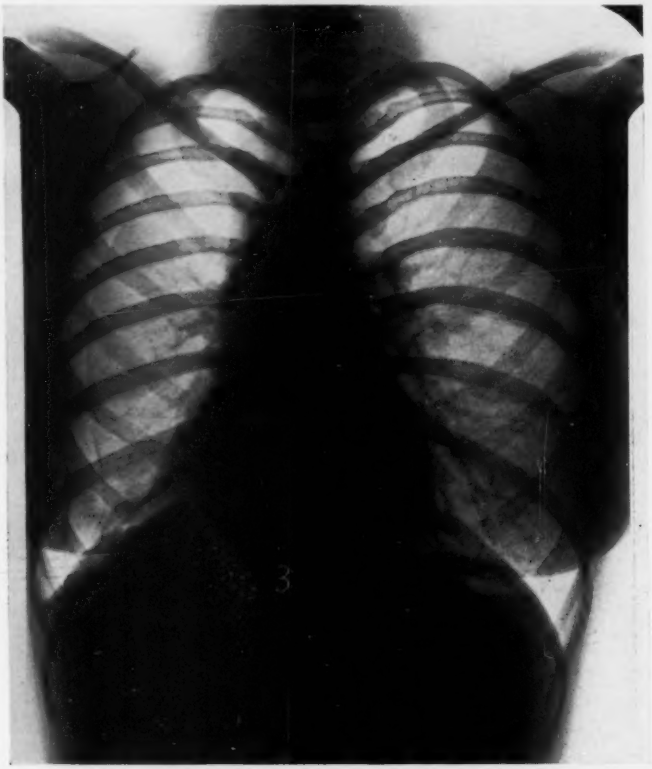


Fig. 3. This plate shows the collapse obtained after artificial pneumothorax was begun on Feb. 13, 1940.

bronchoscopy was decided on to see if by removing the ulcerogranulomatous lesions in the trachea an adequate airway to the left lung could be established.

With this in mind the patient was anesthetized, using a 2 per cent solution of pontocaine injected into the patient under the guidance of a mirror. The patient was then placed on the operating table. She suddenly became very dyspneic and cyanotic. A Mosher life-saver tube was inserted into the pharynx without beneficial effect. An emergency tracheotomy was then done and this afforded temporary relief; however, it

soon became apparent that the obstruction to breathing was below the level of the tracheotomy cannula. The cannula was removed and a 5 mm. bronchoscope inserted into the tracheotomy opening and advanced down the trachea into the left main bronchus. The patient thereupon revived spontaneously. The trachea was filled in its entire extent with tuberculous granulations, making it rather difficult to advance the bronchoscope and to identify the left main bronchus.

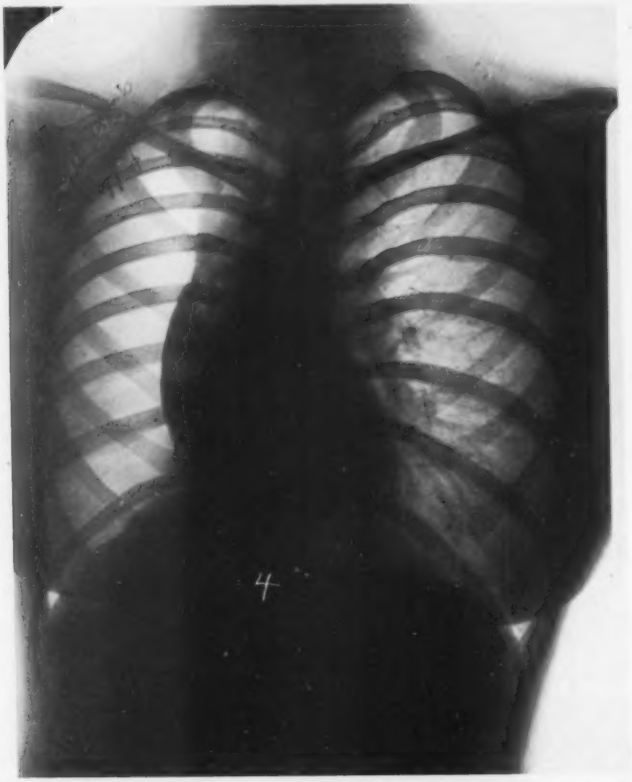


Fig. 4. This plate shows the complete collapse obtained with artificial pneumothorax.

The patient was returned to her room with the bronchoscope in place. The left bronchus was irrigated with 1 per cent ephedrine sulfate in normal saline solution, the excess being removed with the aspirating tube. The following day her breathing was regular and full and she was in excellent spirits; however, her temperature was up to 101° and her progress from this point was gradually down hill. The patient died at 9:05 P. M. on Nov. 21, 1941.

Necropsy was done on Nov. 21, 1941, and excerpts from the report follow:

"The trachea, right and left bronchi are opened posteriorly and the specimen is fixed. The description is made from the fixed specimen. Inspection of the interior of the trachea shows a rather heavy flaky fibrinopurulent and necrotic exudate about the tracheotomy wound. This extends down to the bifurcation. *On the anteromedial wall of the trachea, just above the bifurcation, is a focal area where the tracheal wall is practically destroyed by the inflammatory process.* This appears to extend practically through the tracheal wall. There is an element of stenosis apparently involving the opening of the left main stem bronchus just beyond the carina. This element of stenosis plus the surface exudate appears sufficient to practically occlude the left main stem bronchus."

Final Pathological Diagnosis: Laryngotracheobronchitis, tuberculous, ulcerative with inflammatory stenosis of the left bronchus. Pulmonary tuberculosis, minimal right lung with hilar lymphadenitis, tuberculous pneumonia, acute lobular, artificial pneumothorax right.

In tracing the pathogenesis of this case, Dr. W. A. Smith, Medical Director at Pinehaven, and Dr. Kenneth Lynch, Pathologist, both feel that the onset was a primary complex in the periphery of the right lung which subsequently cleared, leaving some infection, however, in the peritracheal and peribronchial lymph nodes. By direct extension the lining mucosa became involved, producing partial obstruction of right main bronchus and consequent bronchiectasis of the lower portion of the right lung. Even though a good collapse of the right lung was obtained, the tracheobronchial lesions remained, resulting in a gradual decrease in the airway as the granulations encroached on the lumen.

I thank Dr. W. A. Smith and Dr. K. M. Lynch for their valuable suggestions and criticisms in tracing the course of the infection, and also Dr. R. B. Taft for his kind assistance in converting the X-ray plates into photographic form.

VONEDRINE (PHENYLPROPYLMETHYLAMINE). CLINICAL STUDY OF A NEW NASAL DECONGESTANT.*

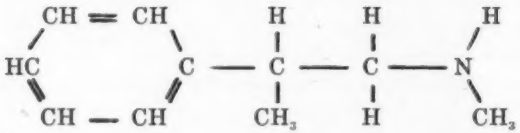
J. S. BUMGARDNER, M.D.; L. D. ABERNETHY, M.D., and F. B. ZIMMERMAN, M.D.,

Louisville.

For the past 2½ years we have used experimentally as nasal decongestant, a new vasopressor amine, Vonedrine (brand of phenylpropylmethylamine). Preliminary clinical results in rhinological practice seemed to indicate that Vonedrine possessed certain advantages over nasal decongestants in common usage both in the form of solutions and inhaler, in that its clinical use seemed to be attended by a noticeable freedom from undesirable local or systemic reactions.

Because of this, we decided to study more closely in a representative series of cases a liquid preparation containing Vonedrine, in comparison to an identical preparation containing ephedrine, and a nasal inhaler containing the volatile Vonedrine base in comparison to one containing racemic amphetamine (Benzedrine Inhaler).

Chemically, Vonedrine is a secondary amine with the following structural formula:



It is a volatile amine, and it forms salts readily with mineral acids, which are stable, readily soluble in water and alcohol, and do not decompose on storage under ordinary conditions of exposure.

---

*From the Department of Otology, Rhinology and Laryngology, University of Louisville School of Medicine and the Louisville General Hospital.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, July 17, 1944.

PHARMACOLOGY OF VONEDRINE.

Warren and co-workers[1] reported a detailed pharmacological and toxicological study of this amine and compared it to ephedrine, a secondary amine, and amphetamine, a primary amine. The latter compound, like Vonedrine, is volatile. Vonedrine was found to have an acute intravenous toxicity approximately equal to ephedrine and about one-third that of benzedrine. On the circulatory and respiratory systems, gastrointestinal tract and isolated uterus of laboratory animals, Vonedrine produced an action quantitatively similar to that produced by ephedrine and amphetamine.

Of marked significance for clinical consideration was the study of the effect of the oral administration of these three compounds on central stimulation, reported by this group. With quantitatively identical dosage orally, amphetamine produced a very marked stimulation. Ephedrine also produced a marked stimulation, but not so great as that elicited by amphetamine; whereas Vonedrine produced no central stimulation.

From these pharmacological studies, it would be expected that Vonedrine would cause a pressor effect in humans. Glaser[2], however, found that Vonedrine, given orally in dosage ranging from 75 to 200 mg. daily over a period of five or six months to 10 individuals, caused no increase in pulse rate or blood pressure and produced no symptoms of central nervous stimulation. Electrocardiographic studies showed no change in the tracing when the patient was under the influence of this drug.

PLAN OF STUDY.

For the appraisal of Vonedrine as a nasal decongestant, two individual plans of study were made: one to determine the clinical efficacy of a liquid preparation containing Vonedrine and its comparison to an identical preparation containing ephedrine, in a series of patients; the other, to study the clinical effect of Vonedrine Inhaler in comparison with Benzedrine Inhaler.

DESCRIPTION OF PREPARATIONS USED.

1. Solution Vonedrine with Ceeprym:

This preparation contains 0.5 phenylpropylmethylamine (Vonedrine brand) combined with levulinic acid; cetylpyri-

dinium chloride (Ceepryn brand) 0.033 per cent and chlorbutanol 0.25 per cent, in an aromatized aqueous isotonic solution with a pH of 5.5.

The Ceepryn in this preparation has been reported to have marked detergent and germicidal qualities,[3,4] with relative freedom from irritating effects upon tissues when used in adequate germicidal strength.[5]

2. Ephedrine Solution with Ceepryn:

This was a special solution furnished as a control for this study, which contained ephedrine sulfate equivalent to 0.5 per cent ephedrine alkaloid; Ceepryn, 0.033 per cent; and chlorbutanol 0.25 per cent in an aromatized aqueous isotonic solution with a pH of approximately 5.6. This solution was identical with the solution containing Vonedrine with the exception that ephedrine replaced the Vonedrine.

3. Vonedrine Inhaler:

This inhaler is of the standard type containing a wick impregnated with 0.325 gm. of the volatile Vonedrine base in combination with small amounts of phenylethyl alcohol, oil of peppermint and synthetic oil of lavender.

(The rate of volatilization of Vonedrine from the Vonedrine Inhaler was studied.[6] An apparatus was set up in which air from the laboratory was first drawn through a sulfuric acid solution to remove any free ammonia. This ammonia-free air was drawn through the inhaler into a measured amount of standard sulfuric acid, where the amine from the inhaler was neutralized and measured. The amount of air drawn per unit of time by a human was measured and found to average approximately 35 cc. per 7.5 seconds of inhalation. This would represent approximately five gallons of air per hour. The amount of Vonedrine carried into the sulfuric acid at various intervals of time was determined and calculated as per cent of total amine present in an average inhaler. Results are shown in Table 1.

TABLE 1. RATE OF VOLATILIZATION OF VONEDRINE FROM INHALER UNDER CONDITIONS APPROXIMATING ACTUAL USE.

Time (minutes)	100	200	300	400	500
Volume of air (liters)	27.7	55.4	83.0	111	138.5
% Vonedrine withdrawn	5%	8.1%	13%	18%	23.3%

Later tests showed that the rate of volatilization was constant until approximately 90% of the total Vonedrine had been withdrawn. From these data, it would evidently require approximately 32 hours of constant air flow at this rate to withdraw 90% of the total Vonedrine from the Inhaler.)

4. Benzedrine Inhaler:

This is a commercially available inhaler containing 0.250 Gm. racemic amphetamine, menthol and oil of lavender.

(In order to compare the rate of volatilization of the Vonedrine and Benzedrine Inhalers, the same procedure was set up as outlined above, with the difference that in order to complete the test within one working day, the rate of air flow was increased to *five* times the rate estimated for actual use. Results of this comparison are shown in Table 2.

TABLE 2. COMPARATIVE RATE OF VOLATILIZATION FOR VONEDRINE AND BENZEDRINE INHALERS UNDER CONDITIONS IN WHICH THE AIR FLOW IS FIVE TIMES THAT ESTIMATED FOR ACTUAL USE.

Time (minutes)	50	100	200	300
Volume of air (liters)	63	126	252	378
% amine withdrawn				
Vonedrine	28%	48%	84%	98%
Benzedrine	34%	60%	84%	93%

It will be seen that the general rate of volatilization of the two amines is roughly parallel.)

METHOD OF STUDY.

1. A group of 50 clinic patients with various rhinological conditions were treated alternately with Solution Vonedrine with Ceepryn and solution ephedrine with Ceepryn in order to compare the two nasal decongestants as to mode of action, length of action, degree of secondary congestion, if any, local tissue reaction and systemic side actions.

2. Solution Vonedrine with Ceepryn was used routinely in office practice in 100 patients as a nasal decongestant by means of spray, swab, tampons, displacement, and for home use between office visits as nasal drops. The cases were not selected, but taken at random, the only consideration being that the patient would return for follow-up inspection and report. The cases were grouped as follows: Group 1, Acute rhinitis, uncomplicated; Group 2, acute sinusitis, complicating rhinitis; Group 3, chronic sinusitis, preoperative, postoperative and unoperated; Group 4, allergic rhinitis.

3. The effect of the Vonedrine Inhaler and Solution on restoring nasal patency in the presence of congestion was tested in a group of 12 patients by photographing the amount of moisture deposited on the mirror of a special instrument by each nostril before and after use of the Vonedrine preparation. The instrument used was similar to the improved nasograph mirror of Glatzel, described by Lieb and Mulinos.[7]

In all cases, the patient was allowed to remain quiet for 15-20 minutes before the test was begun. A nasograph was then made as a "control" before the use of the inhaler or nasal drops. The patient was allowed to inhale through the Vonedrine Inhaler two or three times in each nostril. Nasographs were made after lapses of two and 15 minutes. Similarly, in testing the nasal drops, a "control" nasograph was made, then the nose packed for 15 minutes, at which time the packing was removed and a nasograph made. After a lapse of 20 minutes a third nasograph was made. For these tests the solution was used on tampons, packed into the nose.

4. The Vonedrine and Benzedrine Inhalers were compared in a group of 25 clinic patients with special attention given to: *a.* rapidity of shrinking action; *b.* degree of irritation (sneezing, lacrimation); *c.* local tissue reaction (blanching); *d.* secondary tissue reactions (returgescence, atony); and *e.* systemic side actions (central stimulation, cardiovascular side effects).

5. The Vonedrine Inhaler was used routinely in office practice as a means of maintaining nasal patency between office visits.

6. The inhaler was also utilized by placing the inhaler wick in the container of the Dench bag for inflation of the Eustachian tubes, and the action compared to that of Benzedrine, similarly used.

RESULTS.

1. The comparative use of the nasal drops containing Vonedrine and those containing ephedrine demonstrated that ephedrine acted more rapidly than Vonedrine but the duration of action of ephedrine was shorter than that of Vonedrine. Slightly over 10 per cent of the patients experienced "jitters" from the ephedrine and treatment had to be discontinued. There were no untoward local tissue reactions, "jitters" or other untoward effects observed following the use of the Vonedrine preparation.

2. The results of routine use of Vonedrine with Ceepryn in 100 cases of routine practice showed that in acute rhinitis,

all cases reported no burning from its application, nor did it cause blanching of the mucosa. The rate of decongestion was a little slower than that obtained with ephedrine or Neo-Synephrine, but the duration of decongestion was longer without the rebound congestion that usually occurs with these preparations.

In the acute rhinitis group with complicating sinusitis, there was better drainage with a tendency of the secretions to become less viscid. The mucosa was not blanched by the preparation.

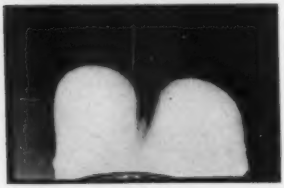
In the chronic sinusitis group, the nasal stuffiness was greatly lessened from the use of one-fourth dropperful bilaterally three times daily. In comparison to other preparations commonly used, there was more prolonged decongestion with improvement from postnasal drip. None complained of burning, a common complaint from these patients when using other nasal drops.

In allergic rhinitis, there was very little response. One of these patients complained of the nose being more congested following the use of the solution.

In all these cases benefited there were no findings that would permit one to say the duration of infection was shortened by an antiseptic. Although sections were not taken in an attempt to study the effect of this preparation on the cilia, there was observed clinically no alteration in the mucous stream, indicating the ciliary function was not entirely inhibited.

3. The group of 12 patients selected for study of the effect of Vonedrine Inhaler and the Vonedrine with Ceepryn upon nasal patency, by use of the improved Glatzel mirror, included cases of nasal congestion caused by the common cold and other rhinological conditions. In every case, a marked increase in the size of the deposit was observed on the nasographs after the use of the Vonedrine preparations.

A characteristic nasograph before and after use of the Vonedrine Inhaler follows (see Figs. 22, 23, 24):

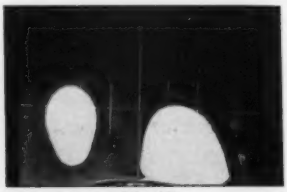


No. 22
Before using inhaler.

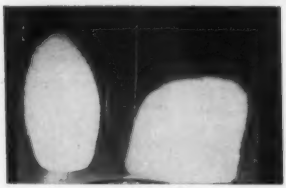
No. 23
Two minutes after two inhalations.

No. 24
Fifteen minutes after two inhalations.

A characteristic nasograph before and after packing with Solution Vonedrine with Ceepryn follows (see Figs. 25, 26, 27):



No. 25
Before packing.



No. 26
Fifteen minutes after packing.

No. 27
Twenty minutes later.

4. Twenty-five patients were treated with the Vonedrine Inhaler and observed for various nasal symptoms, chiefly

nasal congestion. The majority were suffering from the common cold; however, the group included cases of acute and chronic sinusitis and postoperative submucous resection.

All patients with congestion from the common cold reported prompt relief and more comfort, since they were instructed to use the inhaler as often as necessary to secure and maintain a nasal airway night and day. The nasal mucosa was decongested promptly without blanching. There was no effect upon the character or amount of the nasal discharge. Even though the use was frequent in some cases, there were no untoward symptoms, such as irritability, tachycardia or sleeplessness. The absence of troublesome side actions was especially noteworthy in one of the patients who could tolerate the Vonedrine Inhaler but who, upon use of the Benzedrine Inhaler, experienced palpitation and tachycardia.

In acute sinusitis, there was no improvement other than could be attributed to better ventilation and drainage. In chronic sinusitis, results were uniformly poor.

In the postoperative period following submucous resection, results were good, since the convenience of use and the absence of nervous symptoms permitted the patients to maintain nasal patency after the second or third postoperative day.

5. In routine office use, both in the office treatments and as a means of providing comfort to the patient between office visits, Vonedrine Inhaler proved efficacious. Certain characteristic actions of this inhaler compared to others available show: *1*. the nasal mucosa is decongested promptly without blanching; *2*. the duration of decongestion is well prolonged; *3*. no rebound congestion was observed, a clear feeling continues with a gradual return of the congestion in cases of acute congestion; *4*. in dry allergic conditions, sneezing was relieved promptly; *5*. no lacrimation, sneezing or irritation was noticeable; *6*. no sleeplessness or dizziness was reported; *7*. there was no apparent effect on pulse rate or blood pressure; *8*. no nervousness resulted from its use.

6. The Vonedrine Inhaler wick used in connection with the Dench bag for inflation of the Eustachian tubes was advantageous in comparison to the Benzedrine Inhaler wick

similarly used in that: *1.* the feeling of decongestion was much longer in duration; *2.* moisture seemed better controlled; *3.* there was less hesitancy to inflate with moderate inflammation present; and *4.* these treatments were not followed by central nervous stimulation.

COMMENT.

We are aware of the importance of the consideration of nasal physiology, as stressed by Fabricant,[8] in appraising a medication for use in the treatment of rhinological conditions which involves the rather extensive use of vasoconstrictor drugs or nasal decongestants. Accordingly, the choice of a decongestant is most important and the practicability of its use will depend upon its local immediate and secondary actions upon the nasal tissues, the degree of vasoconstriction, the rapidity and duration of action and whether or not its use is attended with systemic side actions upon the cardiovascular or central nervous systems.

Vonedrine, a synthetic vasopressor amine, was selected for study because it seemed to offer certain advantages over some preparations we have used, chiefly its relatively low toxicity in comparison to amphetamine and its effective decongestant action. The field of its clinical application is broadened by the fact that it can be administered as drops, spray or inhalant.

In regard to its local immediate action upon the nasal tissue, it is quite significant in our opinion that it produced on application or inhalation satisfactory rapid decongestion without blanching the mucosa. Burnham[9] has pointed out that the nasal tissues contain two venous plexuses which may undergo vasoconstriction independently or simultaneously. Butler and Ivy[10] have called attention to the significant but often ignored fact that the vascular structure of the nasal tissues is unusual in that it is composed of a superficial capillary layer and a deeper submucosal layer of large erectile sinuses.

In acute rhinitis, for example, vasodilation of the superficial capillary layer results in the characteristic mucosal hyperemia, and vasodilation of the deeper erectile sinuses results in swelling of the turbinates and obstruction of the nasal airway. The chief function, therefore, of a vasoconstrictor agent in such conditions is to cause shrinkage of the

swollen turbinates in order to provide a clear airway. As cited by Butler and Ivy, the hyperemia of the mucosa probably serves the same important functions that hyperemia serves in any inflammatory process in the body and vasoconstriction of the peripheral vascular layer of the mucosal tissue is not a desirable feature in therapy.

It is, therefore, clinically important and advantageous that Vonedrine, applied topically or inhaled, shrinks the turbinates without affecting the mucosal capillaries. Benzedrine, on the other hand, causes immediate blanching of the mucosa, indicating a shrinkage of the mucosal capillaries.

This feature of Vonedrine brings up an aspect of clinical appraisal which deserves comment. Our clinical evaluation of these preparations was based upon actual observation of the tissues and upon subjective response. It was observed that some of the patients initially thought the Vonedrine preparations were not as effective as other preparations while objectively, response was satisfactory. The explanation seemed to be that Vonedrine does not blanch the mucosa and, therefore, there is little stinging upon application or inhalation. Patients mistakenly associate stinging with therapeutic action. It was necessary constantly throughout the study to bear this in mind during the initial treatment of patients in order properly to evaluate the subjective response.

The absence of stinging or irritation on application or inhalation was felt to be one of the outstanding features of this drug.

The solution used in this study contained 0.033 per cent cetylpyridinium chloride, a quaternary ammonium compound with highly detergent and germicidal properties. It is known that compounds of this nature which depress surface tension have a dampening effect upon ciliary activity. In actual clinical use we observed no interference with the mucus stream, which would seem to indicate that the detergent-germicide did not completely inhibit ciliary function. In our opinion, whatever inhibitory effect the Ceepyrn might have on ciliary activity is offset by the detergent and germicidal properties it gives to the decongestant solution.

The detergent or wetting action of the Ceepyrn tends to spread the solution out over the mucosa evenly and inti-

mately. We observed a noticeable decrease in viscosity of nasal secretion following its use. In combination with a decongestant this promoted better drainage.

As to the germicidal properties, we could not demonstrate any definite action upon the condition under treatment; that is, there were no findings that would permit one to say that the duration of the infection was shortened. But in a nasal drop preparation, in the use of which the dropper is inserted into the infected nose and replaced in the bottle, such a germicide will prevent bottle contamination.

As to secondary tissue action, it was observed that Vonedrine in solution decongested the tissues somewhat more gradually than ephedrine or Neo-Synephrine, but the duration of decongestion was much longer and there was no rebound congestion such as usually occurs with these other preparations.

We have observed that when ephedrine is applied to the nasal mucosa repeatedly over long periods of time, there results a dryness and thickening of the tissues. The Vonedrine preparations did not produce this secondary reaction.

An interesting feature of the Vonedrine preparations used was that, when repeatedly and frequently used, they did not produce any stimulating action on the cardiovascular or central nervous system. This is particularly important in regard to the use of decongestant therapy in children and in the use of the inhaler which can so conveniently be used anywhere at frequent intervals.

In none of the cases in this study was there any report of nervousness, dizziness, insomnia or tachycardia following the use of the Vonedrine preparations.

It is possible, from repeatedly frequent use of the Benzedrine Inhaler, to obtain some degree of central stimulation. Some people admittedly use this inhaler for that purpose. There was no essential difference between the decongesting effect of the Vonedrine and Benzedrine inhalers upon the condition under treatment, but the Benzedrine Inhaler produced a central stimulation that tended in some cases to cause slight nervousness and wakefulness. One individual experienced

palpitation from the Benzedrine Inhaler but could use the Vonedrine Inhaler without experiencing this reaction. The absence of central stimulation in the inhaler is important because stuffiness is often aggravated at night and the use of the Vonedrine Inhaler, even upon awakening from sleep during the night, was not conducive to wakefulness.

SUMMARY AND CONCLUSIONS.

1. Vonedrine (phenylpropylmethylamine) is a newly developed vasopressor amine, preparations of which are suitable for use both by topical application and inhalation.

2. Its use as a nasal decongestant in 150 rhinological patients was studied in both clinic and office and its action compared to other decongestants we have used.

3. The Vonedrine preparations used were a solution containing 0.5 per cent Vonedrine and 0.033 per cent Ceepryn in an aromatized aqueous isotonic solution with a pH of 5.5 and an inhaler containing 0.325 gm. Vonedrine combined with small amounts of phenylethyl alcohol, oil of peppermint and synthetic oil of lavender.

4. In the comparative study, special attention was given to local immediate and secondary actions upon the nasal tissues, degree of vasoconstriction or decongestion, rapidity and duration of action and systemic side actions.

5. The Vonedrine preparations produced congestion without blanching the mucosa, a desirable quality in a nasal decongestant for reasons outlined in this report. There was no stinging or irritation upon application or inhalation, one of the outstanding features of this product.

6. Following the decongestant action there was no rebound turgescence or secondary congestion.

7. The onset of the shrinking action was somewhat less rapid than that of some of the other preparations used, but the period of decongestion was of longer duration.

8. The detergent qualities of the solution used seemed to enhance its even distribution over the tissues and to promote drainage by rendering secretions less viscid.

9. There was noted no instance of systemic side actions such as stimulation of the cardiovascular and central nervous systems.

10. Used over relatively long periods of time, the Vonedrine preparations did not produce tissue damage, as determined by macroscopic observations.

11. The effectiveness of Vonedrine both by topical application and inhalation, combined with its freedom from troublesome local or systemic side actions, greatly increases its field of usefulness in rhinological practice as a nasal decongestant.

This work was aided by a grant from The Wm. S. Merrell Company, Cincinnati, and the preparations used in this study were supplied by this firm.

BIBLIOGRAPHY.

1. Warren, M. R.; Marsh, C. G.; Thompson, C. R.:; Shelton, R. S., and Becker, T. J.: Pharmacological Studies on Dl-beta-phenyl-n-propylmethylamine, a Volatile Amine. *J. Pharmacol. and Exp. Therap.*, 79:187-199, 1943.

2. Glaser, K.: Phenylpropylmethylamine Hydrochloride for Asthma. A Clinical Study. *Clin. Med.*, 51:63-65, 1944.

3. Blubaugh, L. V.; Botts, C. W., and Gerwe, E. G.: A Study of the Germicidal Properties of Cetylpyridinium Chloride. New Haven meeting, Society of American Bacteriologists, Dec. 28-30, 1939. Abstracted, *J. Bacteriol.*, 39:51, 1940.

4. Blubaugh, L. V.; Gerwe, E. G.; Botts, C. W., and Helwig, H. L.: Further Observations on the Germicidal Activity of Cetylpyridinium Chloride. Presented before the Society of American Bacteriologists, St. Louis, Dec. 28. 1940. Abstracted, *J. Bacteriol.*, 41:34, 1941.

5. Stitt, H. L.: Bronchial Lavage in Nontuberculous Infections. *Ann. Otol., Rhinol. and Laryngol.*, 52:477-485, 1943.

6. Personal communication: A report from the Research Laboratories of The Wm. S. Merrell Company.

7. Lieb, C. C., and Mulinos, M. G.: Nasograph Mirror of Glatzel as a Measure of Nasal Patency. *Arch. Otolaryngol.*, 30:333-343, 1939.

8. Fabricant, N.: Nasal Physiology. *Am. J. M. Sc.*, 202:601-605, 1941.

9. Burnham, H. H.: Some Differences in the Action of Ephedrine and Epinephrine (Adrenalin, etc.) on the Nasal Turbinate Mucosa. *Canad. M. A. J.*, 27:168-170, 1932.

10. Butler, D. B., and Ivy, A. C.: Method of Application of Drugs to the Nasal Mucosa. A Comparison of Nasal Drops, Sprays and Inhalers. *Arch. Otolaryngol.*, 39:109-123, 1944.

332 West Broadway.

RHINOLOGY IN CHILDREN.
RESUME AND COMMENTS ON THE LITERATURE FOR 1943.

D. E. S. WISHART, M.D.,

Toronto.

In this resumé of the literature pertaining to rhinology in children the same journals have been covered and the same order of discussion has been followed as in previous reviews. A number of papers from other journals have been reviewed. The articles abstracted have been roughly classified under the headings previously used and follow the usual order. Effort has been made to present each writer's ideas fairly and as he has expressed them.

GENERAL ARTICLES ON ACCESSORY SINUS DISEASE IN CHILDREN.

The whole subject of accessory sinus disease is the theme of a long paper by Goldsmith.[1] Although it does not refer specifically to children, it contains much regarding the diagnosis and treatment of sinusitis that is of practical value to the general practitioner and could be made applicable to sinus disease in children.

Riggs[2] believes that the general practitioner as well as the otolaryngologist should recognize that the nasal accessory sinuses may be the starting point for nontuberculous disease of the lungs and bronchi. When patients have indefinite pulmonary symptoms and signs, eradication of an infection in the sinuses will frequently save many months of ineffectual treatment of the lung condition. Very thorough examination of the sinuses is indicated in every case of bronchiectasis; for the latter often begins in patients who had frequent colds in early childhood. By the time the bronchiectasis is demonstrable there may be nothing but postnasal discharge to direct attention to the sinuses. At any stage of this disease the sinus condition must be determined and resolute steps taken

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, Aug. 1, 1944.

to improve whatever pathological condition is found. In the early stages of bronchiectasis further progress of the disease may be prevented — and in the later stages the frequency and severity of reinfection of the bronchial dilatations may be lessened.

Dolowitz, Lock, Haines, Ward and Pickrell[2] state that infections of the sinuses and ears commonly follow acute coryza and physicians are greatly in need of some simple safe method to prevent them. They discuss the common cold, the infections which frequently follow and a means they have evolved of lessening the latter.

Practically all infections of the ears and nasal sinuses are secondary to acute coryza or nasopharyngitis and are due to bacterial invasion. The primary inciting agent may be a virus, but prolongation of symptoms and complications are caused by pyogenic organisms. Nasal and throat culture of large numbers of patients of acute coryza show that the dominating type of organism varies from year to year. Figures and facts are produced which suggest that both acute coryza and acute pharyngitis may sometimes be due to a virus or some agent other than bacteria.

The incidence of nose and throat complications of coryza is steadily decreasing among the general population owing to the widespread practice of the family physician and the pediatrician of giving sulfonamides by mouth for every acute infection of the respiratory tract. One of the objections to giving large doses of these drugs by mouth and thus saturating the entire body to prevent or to cure an infection in one small area is that approximately 30 per cent of the patients develop nausea, dizziness, fever, cutaneous rash or some more serious evidence of sensitivity to the drug. The ideal procedure would be to use bactericidal and bacteriostatic agents locally in minor infections and reserve administration by mouth and by veins for more serious spreading infections. The powder sulfonamides have proved very satisfactory for local application in wounds but are not suitable for infiltration in the nose and throat during acute coryza. Drugs used in the nose should be neither too alkaline nor too acid and must in no way interfere with the movements of the cilia.

Pickrell, in 1941, showed that a large burned area on the skin could be kept far more sterile by frequently spraying it "with a certain solution of sulfadiazine" than by giving sulfadiazine tablets by mouth. The sprayed material is absorbed and the concentration of sulfadiazine in the tissues in a localized area may be six times that in the blood stream; thus the growth of organisms in the sprayed area is inhibited, and further spread of the infection is prevented. This observation is the basis for spraying the nose and throat during the early stages of acute coryza. If the treatment is begun soon after the symptoms of infection appear and is repeated at frequent intervals, the concentration of sulfadiazine in the mucous membrane and lymphoid tissue soon reaches a level that inhibits growth of the bacteria in the region and prevents extension of the infection to the ears and sinuses.

The authors describe a controlled study made during the winters of 1942-1943 in the Johns Hopkins Hospital to test the value of the sulfadiazine spray when used not to prevent the common cold itself but to prevent the complications. The number and the frequency of treatments and the amount of sulfadiazine solution actually sprayed into the nose and throat at each treatment were carefully recorded. As a rule the nose and throat were sprayed from eight to 12 times a day for the first three days and from five to eight times daily for an additional three days. Unless the cough was unusually troublesome the treatment was omitted during the night. Irritation of the skin around the external nares was prevented by frequent application of cold cream or petrolatum. It was during the period of the very first symptoms of an infection of the nose and throat that the best results were obtained. The sulfadiazine spray usually cleared up symptoms of an infection with beta hemolytic streptococci within 24 hours, and occasionally these organisms completely disappeared from the culture after the first day of treatment. Pneumococci and staphylococci were more resistant; but evidently the drug reduces the virulence of these organisms, since the incidence of complication was much less in the treated than in the controlled group. The proper use of the sulfadiazine spray prevents many of the complications of the common cold. The truth of this statement is attested by

the contrast between the incidence of sinusitis, otitis, laryngitis, sore throat and severe cough in the treated group and that in the control group.

Some patients object to the taste, others complain of irritation of the skin around the external nares which can be prevented by frequent application of cold cream or petrolatum. About 3 per cent of the patients were sensitive to the sulfadiazine spray as evidenced by sneezing and increased rhinitis. One patient developed a generalized cutaneous rash. Another patient had definite localized tissue sensitivity.

The possibility exists that general sensitivity may develop in some patients, following local application of sulfonamides for a minor ailment, which might prevent administration of these drugs by mouth for a really serious illness at some future time. No evidence of this was observed, but the subject deserves the consideration and study of members of the medical profession.

Siegle,[4] in 1942, made a preliminary report on the effect of the administration of sulfadiazines at the onset of acute respiratory infection in a group of feebleminded boys at Letchworth Village, N. Y., who are "highly susceptible" to such infections and now has published the clinical data available on the outcome in 162 cases.

Letchworth Village is an institution of the State of New York for feebleminded patients and the children in it are of the lowest mental rating and have an unusual degree of susceptibility to acute infections of the respiratory tract and secondary complications. Eighty-two infections in 74 treated patients were compared with 80 infections in 74 control patients. The patients in the treated group received sulfadiazine as soon as symptoms of respiratory illness appeared.

The initial dose was 0.5 gm. for those weighing less than 50 pounds (23 kg.) and having a temperature of less than 102° F.; all others received 1 gm. The initial dose was followed by 0.5 gm., every four hours for three doses. After that, 2 gm. were used daily, divided into four doses of 0.5 gm. each at 8 A. M., 12 (noon), 4 and 8 P. M. The drug was given for at least four days or until the temperature was less than 100° F. for 24 hours and all signs of infection had

receded. A primary rise in temperature was observed in four infections in patients from the treated group and in 18 in patients from the control group. In two cases in the treated group this rise in temperature was associated with the development of lobar pneumonia. In the treated group, the average duration of fever after the first day's treatment was 1.1 days; in the control group, 3.1 days. A secondary rise in temperature occurred in 11 infections in treated patients and in 22 in control patients. Hospitalization was necessary in four infections in treated patients and in 19 in controls.

In considering the application of the methods used at Letchworth Village to the general population, it should be noted that infection of the respiratory tract is as a rule inordinately common, severe and prolonged among the inmates observed at the institution. Under such conditions, therefore, the use of a bacteriostatic agent, such as sulfadiazine, becomes particularly desirable, whereas administration of this particular drug to the general population would seem to depend on both the subject concerned and the type of infection. Its use should be considered for persons highly susceptible to secondary complications, amenable to the action of the drug and for persons with an infection which is more or less commonly complicated by a serious bacterial invasion such as a severe epidemic form of influenza or of measles. A more generalized application seems inadvisable until more is known about the undesirable effects of sulfadiazine, such as sensitization to it, the toxic effects of its prolonged or repeated use, and the development of strains of organisms resistant to it *in vivo*.

Sulman[5] reports that a suspension of sulfathiazole in an aqueous solution of paredrine hydrobromide has been used in over 75 cases of rhinitis and sinusitis in the course of eight months. It has been successful in reducing nasal congestion and in decreasing or eliminating discharge without evident injury to the cilia. There have been no untoward effects of any kind. Its use has shortened the course of infection for many patients and averted sequelae to colds. The amount employed is so small that it can be used repeatedly without systemic reaction from either the sulfathiazole or the paredrine hydrobromide component.

He states that paredrine hydrobromide in a 1 per cent solution produces a rapid and lasting shrinkage of the nasal mucous membrane and that if 5 per cent of microcrystals of sulfathiazole are added to a 1 per cent aqueous solution of paredrine hydrobromide, a white, practically odorless, suspension is obtained with a pH of 5.5 which does not injure the cilia and does not have any caustic effect.

Suspension of sulfathiazole in an aqueous solution of paredrine hydrobromide was applied by the Proetz method in the treatment of a series of infants up to 5 years of age at St. Vincent's Hospital. These patients were suffering from subacute and chronic rhinitis and sinusitis. Observations were recorded within 24 hours and additional Proetz treatments were given if necessary but not more often than twice a week. Every infant improved. The agreed opinion of the attending physicians and nurses was that 80 per cent of the infants responded more quickly to treatment with the preparation than could be expected with substances previously used. With all but two babies the best results occurred after the first treatment and within the first day. With all but one child the treatments were continued until the condition was satisfactory. This patient had only two treatments during the time allotted to this study. A satisfactory response was obtained within a week except in one case in which four treatments were given in a period of 10 days before a good reaction was shown. The use of the paredrine sulfathiazole combination as many as seven times within three weeks in the Proetz treatment of a 14 months old child and twice a week with babies as young as 5½ and 7 months produced no untoward effects.

The paredrine sulfathiazole preparation instilled into the nose during a cold acts both by constricting the mucosa and by rendering the medium unfavorable for supporting the multiplication of the bacteria which are susceptible to it.

Taylor[6] reports one case in which an upper respiratory infection of five months' duration was definitely cured clinically following the use of a nasal spray of a solution of sodium sulfathiazole and desoxyephedrine hydrochloride. All previous methods of treatment had failed.

COMPLICATIONS OF ACCESSORY SINUS DISEASE.

Simpson[7] states that tables of reported cases show that before the age of 10 years, osteomyelitis of the bones of the skull rarely develops as a result of infection of the frontal sinus. As there is practically no frontal sinus up to the fourth year of life and as it is small for several years thereafter, one could not expect to see this complication arise from the frontal sinus during this period except in rare instances, but it might arise from infection of the ethmoid cells, the antrum or possibly the sphenoid sinus.

In practically all cases osteomyelitis of the skull originates from the frontal sinus and in very few from the ethmoid cells or the antrum. It is his belief that osteomyelitis arises from infection in the sphenoid sinus in many more cases than are reported in the literature. In a large percentage of cases in which the osteomyelitis arises from infection of the sphenoid sinus the condition is discovered at the autopsy table.

Sinusitis arising during the course of influenza, a common cold, scarlet fever, measles and other infectious diseases is the usual precursor of osteomyelitis of the skull.

Osteomyelitis of the skull has been described as developing spontaneously or after an operative procedure on the sinuses. Some authors have reported that in about one-half of their cases the disease developed as a result of an operative procedure. Others have reported a much smaller incidence of this postoperative complication but all emphasize operative procedures as being an important factor in the causation of osteomyelitis of the skull complicating sinusitis. Simpson has seen only one case of osteomyelitis of the skull associated with an operation on the sinuses: in that instance the fact that the chronic sinusitis present was undergoing an acute exacerbation was not suspected before the operative procedure was begun.

It has been said that osteomyelitis may arise after even a very minor operation, as well as after a more extensive procedure. It has always seemed to him that if the operator would remember that only drainage is to be instituted in cases of acute sinusitis, the incidence of the complications,

including osteomyelitis of the skull, would be much lessened. It should also be remembered that opening the frontal sinus through the anterior wall, instead of entirely through the floor, may be a cause of osteomyelitis. In operating on any of the sinuses, especially the frontal, one cannot be too careful in handling the tissues, particularly the bone. The vigorous use of the curette or any use of the rasp is contraindicated.

In all his cases, with one exception, the disease developed spontaneously and had no connection whatever with any operation. He reports 18 cases of osteomyelitis of the skull resulting from infection in the accessory nasal sinuses: of these, eight were children.

Case 1: J. G., a boy, 14 years of age, gave a history of scarlet fever six weeks previously and severe pain and swelling of the right frontal region, with closure of the right eye, four weeks before. Two days later, external drainage of the right frontal sinus was instituted by another surgeon.

When he first saw the patient, there was moderate swelling of the right frontal region and the right eyelid, with a fistula through the skin leading into the frontal sinus. Through this fistula considerable roughened bone could be felt.

With the patient under ether anesthesia, an ethmofrontal operation was done on the right side. The ethmoid cells were filled with swollen polypoid mucous membrane. The middle turbinate was left intact. Practically the entire floor of the frontal sinus had been removed at the previous operation. The sinus was filled with pus and granulations, and the mucous membrane was acutely swollen. The bone of the anterior wall of the sinus seemed to be very rough, as though there had been no mucous membrane on it. There were five sequestra of the posterior wall of the frontal sinus, under which area a portion of the dura about the size of a dime was exposed. The dura seemed to be normal. The wound was left open and was packed with iodoform gauze. The patient made an uneventful recovery.

Case 3: C. J., a boy, 10 years of age, had a history of scarlet fever. Examination revealed slight swelling of the tissue over the left frontal sinus and the lids of the left eye. There was a slight tenderness of the frontal region. He was given ephedrine, and on the following day the swelling was about gone and the tenderness was much less. Conservative measures had been carried out for five days, when the left eye again became swollen.

A Roentgenogram showed pansinusitis on the left side, with a rather large area of decreased density in the anterior wall of the frontal sinus.

With the patient under ether anesthesia, the left frontal sinus was opened. The periosteum was gone from the floor and the entire anterior wall of the sinus. There was a rather large opening through the bone on the anterior wall. The bone was rough over the entire anterior wall and the floor (roof of the orbit). The mucous membrane of the sinus was necrotic, and most of it was detached and lay loose in the cavity. The cavity was full of pus and granulations. The entire floor and the anterior wall were removed. The sinus was packed with iodoform gauze.

The patient made an uneventful recovery.

Case 6: M. E. B., a girl, aged 13 years, had a history of severe frontal headaches for five days, with some swelling around the eyes, especially the right. She had been unconscious for two days.

Examination showed swelling of all the turbinates, stoppage of the nasal passages and considerable yellow pus on both sides. The eyegrounds were normal. Roentgenograms showed increased density of all the sinuses.

With the patient under ether anesthesia, external drainage of the ethmoid and frontal sinuses on both sides was established, with simple drainage of the antrums. There was much pus in all the cavities, especially the left frontal sinus. In 24 hours the patient became conscious. Six weeks later there was swelling of the left frontal region. A Roentgenogram showed an extensive area of decreased density in the left frontal region above and to the left of the frontal sinus. Dr. Francis Murphey, of the neurosurgical division, performed an operation on the region, in which he encountered necrotic bone and an abscess of the left frontal lobe.

The patient had a satisfactory convalescence.

Case 8: J. G., a boy, age 14 years, had a history of having been hit on the head by a baseball one month previously, when he had been unconscious a short time. He had been swimming during the season, the last time one week after being injured by the baseball. There was a history of severe frontal headaches, swelling of the right eye and vomiting, starting five days before admission.

Examination: The right eye was closed. There was moderate swelling of the right frontal region. Pus was present in the right side of the nose. A Roentgenogram showed pathologic changes in the right antrum, but no mention was made of any alteration in the right ethmoid cells or the right frontal sinus, and no fracture lines were seen.

With the patient under general anesthesia, an external incision was made into the right orbit, and a large abscess which extended over the entire frontal region was evacuated.

Treatment with sulfathiazole (2-para-aminobenzenesulfonamidothiazole) was ordered.

Three weeks later a Roentgenographic study was made. Stereoscopic examination of the frontal bone showed a large destructive lesion around the right frontal sinus and above it, involving a large portion of the right frontal bone.

The wound in the right frontal region was reopened, and the entire anterior wall of the frontal sinus was removed. The cavity was packed with iodoform gauze. The bone of the anterior wall of the sinus was worm-eaten and soft, and there was an opening through the anterior wall.

The patient became gradually worse, and Dr. Eustace Semmes, chief of the neurosurgical division, removed the bone of the entire right frontal region and drained a large abscess of the frontal lobe.

The patient died.

Case 11: E. H., a negro boy, 15 years of age, gave a history of having had a temperature varying from normal to 102° F. for four weeks. A diagnosis of malaria was made by his physician, and the patient was given quinine. He was in bed most of the time. The patient had gone swimming all summer. He had lost about 15 pounds (6.8 kg.) in weight and there was a continuous discharge from his nose.

A few hours before coming to the hospital he had had several convulsions, for the first time in his life. These convulsions lasted from 10 to 30 minutes, being of a generalized clonic type. He did not speak after the first convulsion.

Examination: The patient was entirely unresponsive. He did not talk except when forced to inhale ammonia; then he fought and began talking. The results of neurologic examination were all negative A Roentgenogram showed considerable increase in density of both frontal sinuses. Irregular, moth-eaten areas of destruction in the frontal bone, indicating osteomyelitis, surrounded the frontal sinuses and extended approximately 2 inches (5 cm.) beyond them. Sulfanilamide was prescribed.

External drainage of both frontal sinuses was instituted. Each sinus was filled with mucopus. Two weeks later, Dr. Nicholas Gotten, of the neurosurgical division, made a coronal suture incision, uncovered the entire frontal and parietal regions and removed a large sequestrum of infected bone in the midfrontal region, including the anterior and posterior walls of the frontal sinuses. There was considerable granulation tissue between the bone and the dura. Rubber tube drains were inserted.

The patient made a good recovery after the removal of the osteomyelitic bone and two weeks later a complete bilateral external ethmosphenofrontal operation was done. Six weeks later the patient complained of severe headache and nausea. He had a generalized convulsion, lasting 2½ minutes, with no loss of consciousness. One hour later his face began twitching, and he had a clonic convulsion of the left upper extremity, lasting approximately three minutes. Lumbar puncture at this time showed a cell count of 220 cells per cmm., with a spinal fluid pressure of 300 mm.

The department of neurosurgery stated that there was no evidence of abscess of the brain. The department of ophthalmology reported the presence of bilateral choked discs. Two days later, Dr. Nicholas Gotten drained a large abscess of the right frontal lobe, and 10 days later a large rubber drain was placed in the abscess.

The patient has convalesced satisfactorily, without further symptoms.

Case 13: C. T., a negro boy, 14 years of age, gave a history of having had frontal headaches and tenderness of the entire right frontal region, with much discharge from the nose and throat, three years previously. There had been considerable pain and tenderness of the frontal region for the last few weeks.

Examination revealed diffuse swelling and tenderness over and around the right eye. The eye was completely closed. There was a moderate amount of pus in both sides of the nose, especially on the right. Roentgenograms showed increased density of all sinuses.

External drainage of the ethmoid cells and the frontal sinus was instituted. There was much pus in the frontal sinus. Swelling of the orbit and the frontal region continued; six days later an incision was made in the orbit, and about 2 drachms (7 cc.) of pus were evacuated. Through this opening roughened bone could be felt on the roof of the orbit and the anterior wall of the frontal region. Drainage tubes were inserted, and the patient progressed satisfactorily, but pus continued to come from the region of the frontal sinus and three weeks later the sinus was again opened. There was a large opening in the bone of the anterior wall of the right frontal sinus and the cavity of the sinus was filled with granular and polypoid mucous membrane. The opening in the anterior wall was enlarged, all diseased bone being removed. This operative procedure was carried out through a horizontal incision over the cavity of the sinus. The cavity was packed with iodoform gauze. The

wound healed rapidly, and a complete external ethmofrontal operation was done after all inflammatory signs had disappeared, with an uneventful recovery.

Case 14: L. A., a negro boy, 14 years of age, gave a history of pain in the right eye three weeks previously, swelling of the right eye and the right side of the forehead for the last five days and closure of the eye for the last two days. The patient had had a slight cold for one month, but there was no discharge from the nose or throat. The symptoms were so severe that a physician was called 24 hours previously, at which time the forehead was incised.

Examination revealed swelling of the right frontal region just to the right of the midline and extending to the hair line. This region had the appearance of having been incised, and from it pus was exuding. There was swelling of the right eye and pronounced tenderness over the entire forehead. The patient was taken to the operating room the same day, but little was done to the frontal region. He became stuporous within the next day or two; at that time Dr. Francis Murphey, of the neurosurgical division, performed a right frontal craniotomy, with drainage of an abscess of the right frontal lobe. There was extensive osteomyelitis of the frontal bone.

The patient rapidly grew worse and died.

Case 17: R. McG., a boy, 14 years of age, gave a history of having had a blow on the forehead one year previously. A few days later there were swelling and soreness of the forehead with a high temperature. The patient became delirious and was brought to the hospital. Dr. Francis Murphey, of the neurosurgical division, drained subperiosteal and extradural abscesses through a midline opening into the frontal sinus. The patient went home and returned to the hospital eight months later, at which time a Roentgenogram showed osteomyelitis of the skull.

With local anesthesia, Dr. Murphey made a midline incision in the frontal region, uncovering a large sequestrum, which consisted of a portion of the anterior and posterior walls of both frontal sinuses and a large portion of the septum. The frontal sinuses were fairly well cleaned out, but no attempt was made at complete exenteration of these sinuses or of the supraorbital ethmoid cells, which were large and badly diseased.

Recovery was uneventful.

Osteomyelitis is sometimes divided into the localizing and the spreading form which may be fulminating. Simpson thinks that the dividing line is indefinite and that the localizing type may become fulminating and progressive, depending on the resistance of the patient, the virulence of the infection and the form of treatment, or that what starts as a fulminating type may end spontaneously. Certainly anyone who has followed a reasonable number of patients with this condition has seen what seemed to be a minor localized condition change to a fulminating progressive type while the patient was under treatment. He is convinced that the sooner one learns that there is no definite dividing line between the two types and that one should be alert in all procedures of treatment, the better the prognosis will be.

The prophylaxis and treatment of the condition are described in detail. To attempt to summarize these sections of the article would be a mistake on the part of the reviewer. The entire article deserves most careful study.

Blonder[x] states that orbital cellulitis complicating a sinus infection is not uncommon, but orbital cellulitis following an antrum infection is relatively infrequent, according to a review of the cases which have been reported in the literature. The records show that orbital involvement in children results from ethmoid infection more frequently than from infection in the other sinuses. The extension of the infection from the sinuses occurs through venous channels, through dehiscences or osseous necrotic changes in the orbital wall.

A boy, aged 14 years, with proptosis of the right eye and swelling of the periorbital tissues, more pronounced at the lower lid, had a head cold for about two months and a swollen right orbit for about five days before entry to hospital. The conjunctiva was edematous, and moderately injected. No limitation of motion of the eyeball was present. The right naris was filled with thick yellow pus. The face over the antrum appeared full and was tender to palpation. The white blood count was 23,600. The Roentgenological report was that the right antrum was definitely clogged with reactionary osteitis in the floor and medial wall; the right ethmoid was definitely clouded, and extended posteriorly and superiorly to the orbit. The diagnosis was orbital cellulitis resulting from a sinus infection.

The original management was conservative — hot applications, 15 gr. of sulfathiazole by mouth every four hours. Drops of 1 per cent ephedrine solution. Cocaine-ephedrine packs were placed in the middle meatus, followed by suction, several times daily. After five days the proptosis and swelling of the right eye increased and limitation of upward movement of the eyeball developed. The boy appeared increasingly ill. The antrum and the ethmoid were described in the X-ray report as involved. The argument that the antrum was responsible for the complication and not the ethmoid was that there was practically no swelling or tenderness at the inner canthus, and the eye was not directed downwards or outwards; most of the swelling occurred at the lower lid and in addition there was limitation of the eye movement upwards. Considerable tenderness and induration over the antrum was elicited.

Five days after the patient's entrance to hospital under general anesthesia the anterior wall of the antrum was widely removed. The antrum contained about a teaspoonful of fairly thick yellow pus. The pus, granulations and necrotic tissue were removed. The ethmoid cells were exenterated through the antrum to lessen the possibility of reinfection of the already devitalized antrum. No orbital incision was made. An antrum window was made under the inferior turbinate. Subcultures in broth revealed some short chain streptococci and pneumococci.

Postoperatively 15 gr. of sulfathiazole were continued every four hours for five days. Temperature ranged from 100° F. to 103° F. The lower lip became swollen and appeared for a while as though it might suppurate. X-ray examination of the orbital portion of the maxilla at this time

revealed no bone pathology. Limitation of motion of the eyeball disappeared two days after the operation. The proptosis gradually was reduced. On the sixth postoperative day the temperature became normal and recovery was uneventful.

In the discussion which followed, Dr. Howard B. Ballenger stated that he did not recall a definite case of orbital cellulitis secondary to a maxillary sinusitis but said that the late William Mullin was of the opinion that the maxillary sinus was a frequent cause of orbital cellulitis. He had never agreed with Dr. Mullin in that belief. Dr. M. A. Glatt stated that the infraorbital nerve traversed the canal at the roof of the maxillary sinus where the bone is as thin or thinner than the lamina papyracea. In the orbital cavity the canal was incomplete, thus infection of the mucosa can easily penetrate the globe. The author, in closing, stated that he felt extension of the infection occurred through the orbital wall of the antrum because of the marked reaction of that area seen at operation. A fine flexible probe passed in the area of the granulations did not go through the orbital wall. He felt that the limitation of motion of the eyeball upward was due to inflammation of the inferior oblique muscle in the region of the lower lid.

In an article on the treatment of orbital abscess, Ide[9] reports a case of suppurative ethmoiditis in a boy, aged 10 years. There was marked chemosis of the conjunctiva of the right eye, swelling of the eyelids, and tenderness over the inner canthus, but no fluctuating mass. Treatment consisted in application of wet boric acid dressings over the eye and intranasal instillation of 1:10,000 adrenalin, followed by "gentle suction." The patient improved rapidly and recovered completely.

The handling of the diphtheria carrier, states the *British Medical Journal*,[10] is a controversial subject. The procedure should vary according to: *1.* the environmental conditions; *2.* the nature of the carrier state; and *3.* the laboratory facilities available.

1. If a diphtheria carrier is discovered in a family or close community where there are other susceptible children, it is wiser to remove the carrier until the other children have been protected by active or combined active-passive immuni-

zation. On the other hand, isolation of the diphtheria carrier in a day-school where a high proportion of the children have been immunized is probably unnecessary, particularly if the children are under regular medical supervision.

2. The carrier state is with many children a transitory phenomenon, and children with healthy mucous membranes in nose and throat are not likely to be persistent carriers or to spread the infection. Thus, carriers discovered in the routine swabbing of ward contacts are often temporary carriers and should not be transferred immediately to an isolation hospital unless there is some obvious clinical abnormality in the upper air passages. The diphtheria carrier with nasal discharge or diseased tonsils is more dangerous, and should be isolated and treated. There is, of course, no legal power in England and Wales to remove a carrier as such to hospital, but parents usually can be persuaded to do so. While a temporary increase in carriers in place of clinical cases might be expected as a result of immunization (and this happened at Greenwich Hospital School), experience in Canadian and American cities has shown that after a high proportion of the children has been inoculated, the carrier rate among them falls to a very low level.

3. The diagnosis of a diphtheria carrier is a joint responsibility of the physician and the bacteriologist. Swabs must be taken with care from both nose and throat and should be inoculated on a tellurite-containing medium. Organisms resembling C. diphtheriae should be examined biochemically, and, if necessary, by animal inoculation to find whether they are toxigenic. Unless this is done — and in many areas laboratory facilities are still inadequate for the purpose — no reliance can be placed on a report of the presence or absence of C. diphtheriae.

TREATMENT OF SINUSITIS.

Following a review of the pathology, signs, symptoms and findings in sinusitis in children, Tremble[11] states that recent investigations on the properties of nasal secretions make it necessary to alter our view regarding nasal medication. Instead of nasal antiseptics alone it appears more logical to combine mild solutions which are inhibitory to bacteria with those that promote or at least do not retard ciliary activity.

Medication which impairs ciliary activity is harmful as well as drugs which are strongly alkaline or strongly acid. Nasal drops, therefore, should be mildly antiseptic, and have a vasoconstrictor action which does not embarrass ciliary activity: the pH of these solutions should approximate that of the mucous membrane and be isotonic as well as harmless to the nasal mucosa, and finally, they should not produce any systemic or toxic effects.

In the treatment of sinusitis in children, the author employs a combination of sulfathiazole 10 per cent, ephedrine sulphate 1 per cent, and allantoin 0.5 per cent for nasal medication. This suspension is compatible with ciliary action, has a pH within limits normal for the nasal secretion, is almost tasteless, and does not irritate or damage the nasal mucosa. The author claims that over half the cases of sinusitis in children under 12 clear up under postural treatment with nasal medication. Over 25 per cent of cases respond to a combination of nose drops with irrigation of the antrum. Only about one-sixth require antrotomy and this should not be done until the more conservative methods have been given a fair trial.

There is apparently evidence that immunity to typhoid may be obtained by the use of oral vaccines. From time to time one also sees it recommended that oral vaccines are effective for protection against the common cold. What is the present expert bacteriological opinion on the value of prophylaxis against the common cold with vaccines: *a.* injected in the usual way; and *b.* taken by mouth? This question is answered by the *British Medical Journal*[12] thus:

The "common cold" like "influenza" is probably a convenient term to cover a variety of clinically similar conditions of diverse etiology in the upper respiratory tract. There is good experimental and epidemiological evidence that a filterable virus is a causal agent of the common cold, but unfortunately this virus is very difficult to grow artificially, so that a vaccine of it — such as is now available for influenza A — cannot be prepared. On the assumption that certain bacteria, like the pneumonococcus, hemolytic streptococcus, influenza bacillus and the catarrhalis group, are, either primarily or secondarily, causally related to coryzal infection, stock vac-

cines of these organisms have been prepared and used prophylactically. In controlled trials, both in England and in America, these vaccines, given in three or more weekly injections, in the autumn, have failed on statistical analysis to reduce the incidence of the common cold.

Regarding the use of oral vaccines, the evidence that they are effective in protecting against typhoid is flimsy; certainly they do not provoke antibody formation to anything like the same extent as subcutaneous injection of T. A. B. vaccine does. And if there is anything in Besredka's idea of local immunity, sprays or inhalations of anticold vaccines would probably be more effective than oral administration. There is thus no scientific support for the belief that anticold vaccines, given prophylactically either by injection or by mouth, will reduce the incidence of colds in, for example, a group of factory workers.

Harris and Stokes[13] believe that propylene glycol vapor can be used as a practical measure in the control of air-borne cross-infection of the common cold.

Patients in three wards in a children's convalescent home were treated by them by vaporization of glycol vapors in concentrations that had been found by experiment to be bactericidal. Nearly all the children were confined to bed so that there was almost no direct contact. Three wards of the same type were used as controls. The incidence of upper respiratory infection, chiefly common colds, was definitely reduced by glycol vaporization. There were 79 cases of common colds in the control wards and only three cases in the vaporized wards during the period of the experiment. This, they consider evidence that propylene glycol vapor is viricidal as well as bactericidal.

ALLERGY.

Criep[14] reports a case of acquired allergy to argyrol because it is an instance of sensitivity which must be a great deal more common than is recognized and because it offers an opportunity for the study of the possible mechanism involved in drug allergy.

A thorough search of the medical literature failed to reveal more than a single reported instance of allergy to argyrol. (Howard, R. C.: Allergy to Argyrol in a Patient with

Chronic Purulent Otitis Media. THE LARYNGOSCOPE, 40:215-218, March, 1930.) In the one referred to, a young woman received nasal treatment with argyrol for several years twice a week for suppurative sinusitis. Treatments were discontinued for several months and being resumed the patient had an immediate reaction. This consisted of massive swellings of the face, generalized urticaria and symptoms of collapse. On several occasions, subsequent treatment evoked similar severe immediate reaction. Scratch tests with 10 per cent argyrol were positive.

A man, aged 26, had seasonal hay fever for four years, with evidence of considerable infection in the paranasal sinuses. Considerable sneezing, nasal blockage, rhinorrhea and even wheezing would develop during the course of local treatment with the drug. Some time later, spraying of the throat with argyrol for pharyngitis produced severe asthma. It finally became obvious that the patient's discomfort was more than that usually experienced from the mechanical irritation of the nasal tampons; hence local treatments with argyrol were discontinued. Scratch skin tests performed with a weak 1 per cent solution of argyrol produced a definite local reaction. Similarly, an intradermal test with a 1 per cent argyrol solution yielded a very severe local and a mild constitutional reaction. The ophthalmic test was positive with argyrol.

The patient was specifically sensitive to argyrol; first, because of the presence of demonstrable antibodies (reagins in his serum), and, second, because of the development of a constitutional reaction on exposure.

This instance of allergy to argyrol is of interest because, unlike most instances of drug allergy, it is associated with demonstrable specific antibodies. . . The patient did not have any cutaneous reaction to solutions of silver nitrate. It was obvious, then, that the allergy must be due either to the protein vehicle of argyrol or to the combination of argyrol with this protein vehicle.

In view of this information, the patient was tested intradermally with similar dilutions of solargentum (Squibb) and Heyden's U. S. P., mild protein silver. Negative cutaneous reactions and negative passive transfer tests were obtained

with both of these agents indicating that the protein vehicle must be different. Local nasal tampons with both of these preparations failed to give rise to local symptoms or asthma.

It would seem that in both instances referred to, this allergy occurred in otherwise allergic persons who acquired a sensitivity to argyrol following sufficient exposure to this substance.

One wonders whether the supposed rarity of the occurrence of allergy to argyrol in nose and throat practice may not be due to a failure to recognize its presence. Patients receiving such treatment frequently protest about the discomfort it causes them and in many instances it is not easy to recognize this discomfort as an allergic manifestation because the primary symptoms from which the patient seeks relief are so similar to those which develop coincident to treatment. Another instance is that the reaction may be too mild to be recognized. It is, therefore, thought likely that rhinologists who suspect the possible allergic reaction following the use of argyrol may do well to change to some other mild protein silver preparation and avoid these allergic reactions without depriving the patient of the desired therapeutic effect.

These mild protein silver preparations are used very extensively for children and it is generally agreed that the therapeutic effect of all mild protein silver preparations is about the same. In view of this, it may be advisable to change from one preparation to another at stated intervals in the treatment of patients who receive regularly local applications of such preparations and thus avoid the development of allergic manifestations.

Severe reactions to ephedrine are uncommon, but reactions in persons who had previously taken the drug without discomfort are most unusual. The following two cases are described in the *British Medical Journal*.[15]

Case 1: A girl, aged 12, developed a chronic maxillary antritis. In the course of treatment she had often used a spray of 2 per cent ephedrine solution and taken up to ¾ gr. of ephedrine internally in one day. In October, 1940, she had had several treatments by suction technique, in which 1 cc. of 0.5 per cent ephedrine solution was dropped into the nose while she lay with head extended. No adverse effects were observed. In November, 1940, she had a further treatment, in which 1 cc. of ephedrine solution of 1 per cent strength was used. Half an hour later, she felt shivery and dry in the throat. She complained of her heart beating violently, and grew very restless. When seen, she was frightened, flushed and unable to lie still. Her respiration rate was 42 and her pulse rate 180. With sedatives her condition returned slowly to normal in four hours, and next day she was none the worse.

Case 2: This patient, a boy, aged 6, is an allergic type. He suffers frequently from asthma, hay fever and eczema. The family history records allergic conditions on both sides. His mother shows similar reactions to her son's, and his father evinces severe reactions to infections of the respiratory passages. The boy has had ephedrine in various forms, taking up to ¾ gr. a day without ill effect. In April, 1942, he developed a catarrhal infection of the nasopharynx and started to wheeze. He was given ⅜ gr. of ephedrine sulphate combined with ¾ gr. of amytal. (At the age of 4 he had taken half this dose three times in 24 hours without discomfort.) Soon after this administration, however, he became very restless and drank water copiously. His respirations became very rapid and his pulse uncountable. This condition of hyperexcitability slowly subsided, though two hours later his pulse rate was 178 and his respiration rate 40; but after a sedative he went to sleep. Next morning his pulse rate was still faster than normal, but this may have been due to the mild pharyngeal infection.

Such violent reactions to ephedrine in normally tolerant children seem at present to be inexplicable; they are certainly alarming to child, parent and doctor, and show the necessity for care in the administration of the drug.

Wasson[16] reports a study on the efficacy of ethylene disulphonate on a small but intensively observed group of allergic children at a municipal hospital clinic. It had been suggested in 1940 that a departure from normal in the carbohydrate breakdown of the cellular metabolism was the primary cause of the allergic state and was due to the absence of certain catalysts of coenzymal activity in the body. British and Belgian observers had suggested that the normal cellular carbohydrate metabolism of the allergic individual could be restored by a provision of a suitable oxidation catalyst. They found that ethylene disulphonate in a proper dilution fulfilled the requirements of such a catalyst, though no claim was made that the substance itself was present in a normal healthy body. Twenty treated and 20 control patients were carefully studied and the data obtained are presented in many charts. The dosage of ethylene disulphonate used is not stated.

The ethylene disulphonate was administered by intramuscular injection into the gluteal muscle in infants, and into the deltoid in older children. It was followed by an acute pain lasting for no more than two minutes and immediate visible fibrillation of the injected and adjacent muscles for not more than two minutes. Not a single patient complained of any undesirable local or general reaction following the injection.

For a week before and two weeks after the injection of ethylene disulphonate, patients were instructed to take a

strictly lactovegetarian diet, and to avoid coal tar, opium, and barbiturate derivatives.

A saline cathartic was given on two successive nights prior to the injection.

Following the injection, each patient was told to report to the clinic in two and in nine weeks. If no improvement occurred more injections were given; however, such cases were few. The average number of injections per patient between November, 1941, and the end of May, 1943, was 1.5.

In the 20 patients treated with ethylene disulphonate, 11 were completely relieved of symptoms and only two experienced no relief.

In a control group of 20 patients treated by routine methods and whose symptoms were less severe at first, only six were completely relieved, and 10 had no relief.

Relief from symptoms in some instances had been prolonged and is continuing. Most patients have been able to carry on normal activities and have enjoyed an unrestricted diet. The author considers that the results justify a more extensive study.

The Chairman of the Medical Advisory Committee, Asthma Research Council, England, Sir Arthur Hurst,[17] discusses asthma in childhood with interest stimulated by a personal acquaintance with the affliction. Included in his remarks are a few statements concerning its association with allergy which merit thoughtful consideration.

He points out that associated with the physical side of the asthma diathesis there is probably a psychological side which manifests itself in a special type of personality. It is extremely difficult to decide how much of the asthma personality is the result of over-protection by too anxious parents and how much is constitutional. The constitutional factor in asthma shows remarkable variations at different times. A patient may be almost constantly asthmatic for weeks and then have a period of complete freedom, when he can expose himself with impunity to all the allergens to which he is usually sensitive. It is often impossible to recognize what leads to these periods in which the bronchial system appears to have lost its irritability

but there is no doubt that the more completely attacks are prevented by removing all known existing causes the less irritable does the bronchial system become. If a child can be kept completely clear from asthma for a couple of years he is quite likely to remain free for the rest of his life.

In recent years so much attention has been directed to the question of hypersensitiveness to proteins and other chemical substances in asthma that there has been a tendency to regard allergy as the one essential factor. The truth is, however, that an individual who is hypersensitive to one or more proteins does not suffer from asthma unless he has the asthma diathesis. . . There is no doubt, too, that many asthmatics are not allergic at all, their attacks being caused only by reflex and physical stimuli.

In the last 23 years I have had an extensive experience of the skin tests which have been applied by various experts but never by myself. The results have been profoundly disappointing as, with two or three exceptions, they have never revealed an allergen responsible for a patient's asthma that had not already been recognized by careful cross-examination. On the other hand, on several occasions I have been told that a positive reaction was obtained with a food which the patient rarely or never ate or with the emanation of an animal or a pollen with which he never came into contact, and in other cases no reaction was obtained with an allergen to which the patient was proved to be sensitive.

The respiratory tract is the main reflex source of asthma. When a child with a narrow nasal airway lies down at night the passive congestion of the tissue of the turbinals may be sufficient to bring them into contact with the irritable mucosa of the septum and thus give rise to reflex bronchial spasms. The narrow airway may be congenital or the result of an injury or of chronic infection which leads to permanent congestion of the mucous membrane and the development of polypi. Intermittent congestion is also a common reaction to the inhalation of allergens. Suitable treatment, with a minimum of surgery, may prove very beneficial and no asthmatic child should be allowed to remain a mouth breather.

The most common exciting psychological cause in asthma is expectation. The bad influence of the home on many asth-

matic children is, to a great extent, a reflection of their parents' anxiety. It is the psychological rather than the allergic atmosphere from which they need to be removed. The child should not be pampered but be encouraged to lead as normal a life as possible. He should be kept in bed for bronchitis but not for asthma.

In 1902, a specialist from overseas, having cured 347 of his 402 asthmatic patients by cauterizing what he regarded as an asthmogenic point on their nasal septa, settled in London. He was at first successful with the 80 per cent of his cases with normal looking noses, the remaining 20 per cent being the unhappy people with abnormal noses, often in part the result of surgery. Forty years have passed since then and this method of treatment is almost forgotten, having given place with success to at least a dozen other specific treatments, each with its 70 or 80 per cent of cures. All these forms of treatments produced approximately the same percentage of temporary cures. They are so diverse in nature that the only thing they have in common is the faith their exponents have in them, a faith which is transferred by suggestion to the patient with sufficient strength to be successful in about 75 per cent of cases. Unfortunately the asthma diathesis remains unaffected so that recurrence is just as frequent as after spontaneous remissions.

Expiratory exercises should not be regarded as a substitute for walking and open air games but as a form of training. Nothing is more undesirable than prohibiting games. An asthmatic child should be taught to regard his asthma as an inconvenience but not as a disease. Asthmatic children should be encouraged to have a cold bath every morning all the year round or at least a cold douche after a hot bath of very short duration.

TONSILS AND ADENOIDS.

The reaction in recent years against wholesale tonsillectomy, states the *Lancet*[15] in an editorial, is based principally on the findings that tonsillectomized children are no more resistant to sore throat, otitis media, rheumatism and nasopharyngeal infections than are children who still have their tonsils. This, of course, does not exclude the possibility that but for tonsillectomy the former group might have had a

higher incidence of these infections, nor does it mean that tonsils that are obviously diseased and a predisposing cause of frequent sore throats should not be removed. But there seems no justification for the practice, common particularly among well-to-do families, of excising enlarged tonsils as such. Indeed, it now seems probable that the tonsil by trapping pathogenic bacteria not only may act as a front-line guard against infection, but may also contribute to the production of antibodies specific against the invading microorganisms. Enlargement of lymph-glands in response to infection is commonplace, and is not as a rule accompanied by increase in blood lymphocytes. On the other hand, experiments by a number of independent workers have supplied evidence that antibody is produced in the lymph-glands and that the germinal centers of lymph-glands appear in young animals as a direct response to the injection of antigenic material like bacteria or toxins. The cells in the germinal center are, according to Maximow, primitive mesenchymal cells which may readily take on the function of phagocytic histiocytes. Enlarged tonsils and adenoids in children, therefore, may be interpreted as part of the body's reaction to the many foreign bacterial acquaintances which the child makes in early life.

A study by Rantz and his co-workers on the presence and persistence of specific antibodies in streptococcal throat carriers, some of whom had their tonsils removed, supplies some apposite data. Examinations were made for the presence of type-specific streptococcus agglutinins and for antistreptolysin in the blood of 64 children, 33 of whom were later proved by culture of the excised tonsils to be carriers of group A hemolytic streptococci. Incidentally, only half of these streptococcal carriers were detected by pretonsillectomy throat cultures. Among the carriers, 85 per cent had an appreciable titer of type-specific agglutinins and 70 per cent had antistreptolysin levels of 100 units or more, which may be compared with figures of 13 per cent and 38 per cent, respectively, in the noncarrier group. After-tonsillectomy follow-up studies for one to three months in 21 carriers showed a definite fall in the level of antistreptolysin in 19 cases; there was no corresponding fall in streptococcus agglutinins. Interpretation of these findings is not easy. The higher anti-

body levels in the carrier group before tonsillectomy may have been due to the persistent stimulus from the hemolytic streptococci harbored in the tonsil, or may have occurred in response to a recent infection, although the histories did not suggest that this was so. The quick and consistent fall of antistreptolysin in patients after tonsillectomy differs from the usual findings in patients after an acute streptococcal infection where the titer is maintained at a high level for six months in about half the cases. Thus the reduction in circulating antibody is presumably to be correlated with the removal of the antigenic stimulus in the tonsil. Whether the tonsil itself was contributing to the production of antibodies is doubtful, but the foregoing evidence that this tissue may constitute an important section of the antibody factory and the old observation that streptococcal carriers are resistant to fresh infection may further impress the family doctor and his surgical colleague with the need for a conservative attitude towards the enlarged tonsil.

This editorial evoked the two letters which follow.

Your leader, wrote Leathart,[19] shows a welcome spirit of tolerance for the pharyngeal lymphoid tissue. All tonsils except those of the newborn child contain living micro-organisms, picked up from food or air or both. Many of these oganisms die, and to these the child is immune; others, to which he is not immune, live and produce toxins. From the tonsil these toxins pass to adjacent lymph nodes, and thence by efferent lymphatics to the tissues, evoking the formation of antibodies. The blood stream carries the antibodies to the tonsil to destroy the organisms, the surplus antibodies remaining in the blood. The tonsil is, therefore, an inoculation organ through which immunity is built up and the child enabled to resist the infections current in the community in which he lives. Few children, if any, are born immune to all food or air-borne infections; most of them have to pass through many such infections before healthy adult life is reached. An attack recovered from may, therefore, be regarded as a stepping stone towards increased immunity. The same duties are shared by the adenoid mass and the lymphoid follicles scattered about the mucous membranes of the body, including the Peyer's patches (which, of course, deal mainly with food-borne infections).

The crypts of the tonsil, however, form ideal breeding places for organisms, and though no such crypts are present in the adenoid mass, it contains spaces between its folia in which organisms can lodge and multiply. Because of their size and structure the tonsils and adenoids are a more important section of what you have called the antibody factory than the smaller lymphoid follicles scattered about the mucous membrane. During childhood, then, they have important work to do which is interrupted by their removal; and unless they are harboring an organism to which no further immunity is possible they should be left where they are.

Reasons usually given for removal of tonsils are: recurrent sore throats; and tonsillar sepsis or enlargement. If sore throats are an essential phase in the acquirement of immunity, removal for this reason cannot be justified. There are no different degrees and forms of sepsis, but it is impossible to assess these by inspection. In the sense that they all carry micro-organisms, all tonsils are septic; but the mere presence of organisms does not tell us that the production of antibodies has ceased. Large tonsils have been accused of hindering breathing and swallowing, but these are imaginary dangers. It is quite common to see a perfectly healthy child with very large tonsils, and mere bulk does not imply failure in performance.

Three main reasons given for the removal of adenoids are: mouth-breathing; recurrent colds; and discharging ears. The adenoid mass, like the tonsils, enlarges when it is inflamed, and in that state might block the airway; but the condition is temporary, and the adenoid mass must rarely be large enough to obstruct breathing at other times. At operations on children for nasal obstruction it is not uncommon to find the adenoid mass quite small; such children, however, usually have a mucus or mucopurulent nasal discharge coming not from the adenoids but from the sinuses. In most of these cases transillumination shows an opaque sinus on one side or both. Sinusitis is accompanied by enlarged turbinals and these usually cause more obstruction when the child is lying down than when he is standing, so that the noise of obstructed breathing is more troublesome at night than in the daytime. Nasal obstruction in children, then, is often due to recurrent enlargement of the turbinals, which in turn may be due to

an infected ethmoid labyrinth. Small doses of potassium iodide (gr. ½-3, depending on the age of the child) stimulate the mucous glands of the nose and drain the sinuses by increasing secretion. Like recurrent sore throats, recurrent colds have their place in the process by which immunity is acquired; so that they do not indicate adenectomy. Removal of adenoids is sometimes successful in reducing or stopping aural discharge in subacute or recurrent cases, many of which would have recovered in any case. In chronic cases it usually fails. Primary acute otitis, on the other hand, often follows removal of adenoids.

The main function of the tonsil and adenoid mass, then, is to pick up organisms from food and air or both, and to grow those to which an immunity is required. Until it is evident clinically that they contain an organism to which immunity is impossible, it would appear unwise to remove them.

Layton[20] commented that the authority of the columns must be welcome to those who believe that too many tonsils are still taken out. But certain terms need amendment to secure proper action. "Enlarged" and "obviously," with "chronic tonsillitis," should be expunged from our terminology.

"Enlarged" infers comparison with a normal. No one ever has described the size of a normal tonsil and no one ever will. To do so he must take into account the size of the subject, his age, the shape of the pharynx, the amount of lymphoid tissue there and in the body generally, the hygiene and ventilation of the home, personal and domestic cleanliness, room space accommodation, nutrition and clothing, as well as exposure to droplet infection and tendency to infection. The attempt would be an impossibility. The terms used to be applied to those vast masses that once obstructed respiration and that have passed away. Then in what other part of the body does anyone remove an organ on the diagnosis of "diseased" without trying to define the pathological condition? "Obvious" is a danger to the clinician; it makes him feel that there is within him some God-given power of divination, instead of reminding him that he must settle down to consider every factor.

The problem is to assess the reactions of a single mass of lymphoid tissue to the hygiene of the subject having regard to the other masses of lymphoid tissue near the site and in the rest of the system. It resolves itself in any given case into trying to decide whether the organisms within the tonsil are neutral to the host or whether they are living in the crypts in a state of true or false symbiosis; for it is only in the last case that tonsillectomy is effective. Pretonsillectomy throat cultures merely pick up organisms which are on their way to be destroyed in the tonsil while being conveyed there by the ciliary action of the nose.

To say that unnecessary tonsillectomy is common particularly among well-to-do families suggests that medical men allow their judgment to be swayed either by the wish of the layman or by the desire for gain. Attempts are certainly made by parents to urge a doctor to advise this operation; and in borderline cases — and there are many — weight should be given to this wish. In a case where the balance of evidence is against operation, the advice to wait six months will usually be taken. Rich or poor, they sometimes go to someone else. That the financial factor is not the cause is shown by the fact that the greatest excess is among those children who are dealt with under the Children Acts of 1906 and 1918.

Some health officers strive to control the habit of tonsillectomy among their staffs. The question arises, how much the administrator may use his power to guide the clinician, but it should be possible to draw up administrative instructions which would have the effect of eliminating unnecessary operations without interfering with the judgment of the true clinician.

He pays tribute to one who cannot speak for himself since he is in the hands of the Japanese — Prof. K. H. Digby, of Hong-Kong. In 1919, when many were saying that the tonsils were a useless relic devoid of function, he put forward on anatomical and clinical grounds the view that not only were they filters to the entry of organisms into the body, but also that they had a definite function in raising the acquired resistance by the production of antibodies (Immunity in Health, London. See also *Lancet*, 1823, 11, 1077).

The reference which follows is an illustration of the doubts which one often hears expressed by medical men of discernment but which, on this continent, are rarely stated in print.

Paton[21] analyzed the records of girls admitted to a boarding school between 1930 and 1939. Fifty-seven per cent of the girls had had their tonsils removed, and 50 per cent had had their adenoids removed. On arrival at school the operation group was no healthier than the control group. While at school the operation group was less healthy than the control group: as shown by the number of school days lost through illness. The operation group suffered less from tonsillitis; they suffered much more from respiratory infections and lost more days from bronchitis alone than they gained in respect of tonsillitis. From the data, Paton makes certain deductions: removal of the tonsils is the factor in the combined operation responsible for the reduction in tonsillitis and for the increase in respiratory infections; adenoidectomy alone reduces the liability to respiratory infections. In the combined operation group the removal of adenoids failed to counteract the increase in respiratory infections which resulted from the tonsillectomy; removal of adenoids increases the liability to acute otorrhea; recurrent attacks of otorrhea are seldom prevented and primary attacks of otorrhea are more frequent after the operation.

ATROPHIC RHINITIS AND OZENA.

Wagers[22] reports 26 cases of atrophic rhinitis treated with estrogenic substance; 11 of these patients were males and 15 females; ages ranged from 6 to 72 years. Ozena was present in 13 cases. The patient visited the clinic once a week and the nasal passages were thoroughly cleaned and the estrogenic preparation amniotin (Squibbs) was applied to the nasal mucous membrane. The patient was given a supply of amniotin to be sprayed into each nostril after irrigating each nasal passage with two quarts of warm saline solution to which 4 gm. of sodium bicarbonate had been added. Cleansing was done and an estrogen spray was used three times daily for eight to 12 weeks, then daily for two weeks. The estrogen treatment was then discontinued, but the patient was instructed to irrigate the nose once daily. Six patients showed marked improvement and 12 patients showed mod-

erate improvement, while eight patients showed no improvement. While this article hardly refers to children, it is mentioned because it records a variation of the estrogenic treatment of atrophic rhinitis which would be possible to use for children suffering from this disease.

SURGERY.

Proetz[23] has written an article on planning nasal surgery to which justice cannot be done in a mere resumé. The complete article should be read. He states that the logical end to which all treatment should be directed is ultimate improvement in function; in function first and last. The surgical fashion, whether it be of the moment or a relic of a previous era, is of no importance. The patient's measure of a successful treatment — and it should be the physician's — is a nose that functions, a nose of which he is not conscious. Consequently there should be individual planning for practically every case. How this end is to be accomplished should be definite in the mind of the operator at the start, so that he may not by inept surgical methods set up new disturbances.

The nasal functions which must prevail in the end in order to establish a working nose are olfaction, adequate humidification and heating, filtration and the ability of the membrane to keep itself clean through an active and effective ciliary mechanism.

He points out that the surgeon has the choice of: *1.* no intervention at all; *2.* operation for ventilation; *3.* operation for relieving mechanical pressure; *4.* operation for drainage; *5.* operation for eradication of diseased tissue.

Allergic membranes after removal will presumably be replaced with other allergic membranes, since allergy is an attribute of the person and not a local disorder. In his experience, allergic tissues should be regarded surgically on the basis of their potentialities aside from allergy. They should be removed if they obstruct or if a concurrent infection demands it. Far from constituting a contraindication to surgical intervention, allergic symptoms in the nose and chest are often alleviated by a judicious re-establishment of something approaching physiologic airways. He is aware that

sometimes operation has aggravated symptoms and has permitted fresh sensitization. The patient should be guarded against this by choice of location and season.

TUMORS.

Ellis[24] reports the history of a girl aged 12 who had an unusual type of adenocarcinoma arising from the anterior ethmoid region. As far as he is able to determine, the patient is the youngest on record with this type of carcinoma; the result of his operation is still favorable, there being no indication of a recurrence after nearly two years. The article is illustrated with photographs of the patient before and after operation and a photomicrograph of a section of the tumor.

The chief complaint was frequent and repeated nose bleeds with some spreading of the base of the nose on the left side. Daily bleeding had been noticed for five weeks before the child was taken to the family physician. He found a growth in the left side of the nose which he diagnosed as a polyp. Several biopsies were made, the original diagnosis being pyrogenic granuloma with no evidence of malignancy. The tumor was removed through an external ethmoid incision and the raw surfaces in the nose were cauterized by electrocoagulation. The tumor consisted of a friable mass which practically filled an ounce medicine glass. It filled the anterior ethmoid cells and involved the nasoantral wall. The pathologist's report was papillary adenocarcinoma grade 2.

This patient has been watched closely since her dismissal from the hospital, but no tissue which even looks suspicious has yet been seen. The patient is gaining weight and is in normal health at present.

Such cases as the one reported should serve as a reminder that many such tumors are not beyond help. One must remember that when the tumor can be entirely removed and when there has not been any metastasis the patient can be cured.

BIBLIOGRAPHY.

1. Goldsmith, Perry G.: Accessory Sinus Disease in General Practice. *Canad. Med. Assn. Jour.*, 426, May, 1943.

2. Riggs, R. H.: Sinusitis in Diseases of the Lower Respiratory Tract. *New Orleans M. and S. Jour.*, 475, April, 1943.

3. Dolowitz, David, A.; Lock, Walter E.; Haines, Henry L.; Ward, Arthur T., Jr., and Pickrell, Kenneth L.: The Prevention of Ear and Nasal Complications of the Common Cold. *Jour. A. M. A.*, 534, Oct., 1943.

4. Siegel, Morris: Studies on Control of Acute Infections of Respiratory Tract; Oral Administration of Sulfadiazine at the Onset of Acute Respiratory Illnesses. *Am. Jour. Dis. Child.*, 114, Aug., 1943.

5. Sulman, Louis D.: Paredrine Hydrobromide-Sulfathiazole Therapy of Infections of the Upper Respiratory Tract. *Arch. Oto-Laryngol.*, 713, May, 1943.

6. Taylor, H. W.: Treatment of Case of Persistent Upper Respiratory Tract Infection. *Arch. Pediat.*, 565, Oct., 1943.

7. Simpson, W. Likely: Osteomyelitis of the Skull Resulting from Infection in the Sinuses. *Arch Oto-Laryngol.*, 463, April, 1943.

8. Blonder, Edwin J.: Orbital Cellulitis Complicating a Maxillary Sinusitis. *Ann. Otol., Rhinol. and Laryngol.*, 524, June, 1943.

9. Ide, David: Suppurative Ethmoiditis with Special Reference to Orbital Abscess and Its Treatment. The Laryngoscope, 53:50, Jan., 1943.

10. Answer to Question, What to Do with Bacteria Carriers? *Brit. Med. Jour.*, 596, Nov., 1943.

11. Tremble, G. Edward: The Conservative Treatment of Sinusitis in Children. *Canad. Med. Assn. Jour.*, 496, Dec., 1943.

12. Letters, Notes and Answers: Vaccines for Common Colds. *Brit. Med. Jour.*, 221, Aug., 1943.

13. Harris, T. N., and Stokes, Joseph, Jr.: Air-Borne Cross-Infection in the Case of the Common Cold; a Further Study of the Use of Glycol Vapors for Air Sterilization. *A. M. Sci.*, 631, Nov., 1943.

14. Criep, Leo H.: Allergy to Argyrol. *Jour. A. M. A.*, 421, Feb., 1943.

15. Memorandum: *Brit. Med. Jour.*, 414, Apr., 1943.

16. Wasson, Valentina P.: Ethylene Disulphonate in the Treatment of Allergic Children. *Arch. Pediat.*, 511, Sept., 1943.

17. Hurst, Sir Arthur, M.A., D.M., F.R.C.P.: Asthma in Childhood. *Brit. Med. Jour.*, 403, April, 1943.

18. Editorial: The Tonsils and Antibodies. *The Lancet*, 575, Nov., 1943.

19. Leathart, P. W.: Letter to the Editor. *The Lancet*, 619, Nov., 1943.

20. Layton, T. B.: Letter to the Editor. *The Lancet*, 651, Nov., 1943.

21. Paton, A. H. P.: Tonsil Adenoid Operation in Relation to Health of Group of School Girls *Quart. Jour. of Med., Oxford*, 119, Dec., 1943.

22. Wagers, Arthur J.: A Consideration of Atrophic Rhinitis and Its Treatment by the Use of Estrogenic Substance. The Laryngoscope, 53:39-45, Jan., 1943.

23. Proetz, Arthur W.: On Planning Nasal Surgery. *Arch. Oto-Laryngol.*, 502, April, 1943.

24. Ellis, Bert E.: An Unusual Nasal Tumor. *Arch. Oto-Laryngol.*, 38, July, 1943.

170 St. George Street.

IN MEMORIAM

SAMUEL IGLAUER, M.D.,

1872-1944.

It is with deep regret that we record the death of Dr. Samuel Iglauer on June 23, 1944. He died of cerebral hemorrhage in Cincinnati, at the age of 72. So passes from our midst another of the highly respected pioneers in otolaryngology.

Samuel J. Iglauer was more than a pioneer; he was almost a tradition. His friendly countenance and quiet but cordial greeting were unfailing accompaniments at almost every national gathering of specialists where he appeared regularly on the programs and where his contributions were valued for their originality and clear thought.

Early in his medical career, Dr. Iglauer became interested in diseases of the ear, nose and throat, and his early study was supplemented by work in Vienna in 1900.

Twenty years ago he became engrossed in bronchoscopy and plastic surgery and in these fields his work was of conspicuous excellence. The field of teaching was also a congenial activity and the large number of students who came under his tutelage loved and revered him. In recent years he conducted a successful postgraduate course at the Cincinnati Medical School each spring, and was also professor of otolaryngology there.

He was the author of numerous medical monographs, a member of the American Medical Association, American Laryngological, Rhinological and Otological Society, Ameri-

can Academy of Ophthalmology and Otolaryngology, American Broncho-Esophagological Association, American College of Surgeons, Cincinnati Otolaryngologic Society, American Academy for the Advancement of Science, Ohio Public Health Association and an honorary member of the Kansas City Society of Ophthalmology and Otolaryngology.

Dr. Iglauer was a man of varied interests and culture. While the practice of his profession and its allied subjects were his major interests, he found time to serve the Cincinnati community in many different channels. He was a member of the Cincinnati Charter Commission and was a Captain in the first World War.

Unobtrusive and modest, simple in his tastes, a lover of art and music, full of kindly humor, — he was a gracious and friendly addition at all social gatherings and could become eloquent over his particular athletic outlet — golf.

Taken all in all, Dr. Iglauer was an honor to his profession, devoted to his patients and colleagues; a man of outstanding medical attainment whose passing leaves a void that will not easily be filled.

His widow, Mrs. Helen Ransohoff Iglauer, two daughters and two grandchildren survive him.

DIRECTORY OF NATIONAL OTOLARYNGOLOGIC SOCIETIES.

AMERICAN OTOLOGICAL SOCIETY.

President: Dr. Gordon Berry, 36 Pleasant Street, Worcester, Mass.
Secretary: Dr. Isidore Friesner, 101 E. 73rd Street, New York.

AMERICAN LARYNGOLOGICAL ASSOCIATION.

President: Dr. Charles J. Imperatori, 108 E. 38th Street, New York.
Secretary: Dr. Arthur W. Proetz, Beaumont Building St. Louis.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, INC.

President: Dr. Albert C. Furstenberg, University Hospital, Ann Arbor, Mich.
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Building, Rochester, N. Y.

SECTIONS:

Eastern—Chairman: Dr. Oram R. Kline, 414 Cooper Street, Camden, N. J.
Southern—Chairman: Dr. Verling K. Hart, 106 W. 7th Street, Charlotte, N. Car.
Middle—Chairman: Dr. Carl H. McCaskey, 608 Guarantee Bldg., Indianapolis, Ind.
Western—Chairman: Dr. Aubrey G. Rawlins, 384 Post Street, San Francisco, Calif.

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON LARYNGOLOGY, OTOLOGY AND RHINOLOGY.

Chairman: Dr. Louis H. Clerf, 1530 Locust Street, Philadelphia.
Secretary: Dr. Fletcher D. Woodward, 104 E. Market Street, Charlottesville, Va.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. Lawrence T. Post, 508 N. Grand Boulevard, St. Louis.
President-Elect: Dr. Gordon B. New, Mayo Foundation, Rochester, Minn.
Executive Secretary: Dr. William L. Benedict, Mayo Clinic, Rochester, Minn.

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION.

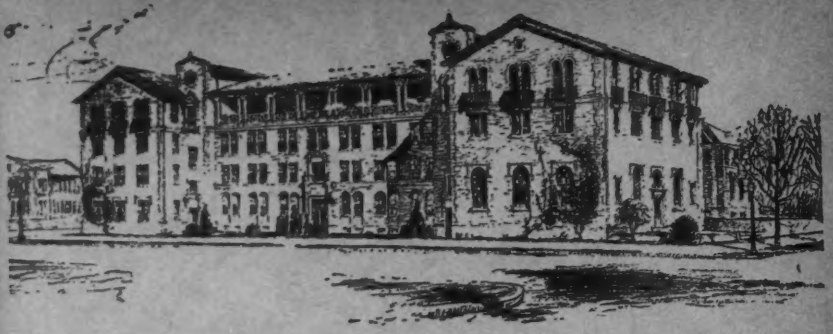
President: Dr. Carlos E. Pitkin, Carnegie Medical Building, Cleveland, Ohio.
Secretary: Dr. Paul Holinger, 700 N. Michigan Avenue, Chicago.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. M. E. Trainor, 523 W. 6th, Los Angeles.
Vice-President: Dr. Kenneth Brandenburg, 707 Security Building, Long Beach, Cal.
Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central, Glendale, Cal.
Committeewoman: Dr. Etta C. Jeancon, 523 W. 6th Street, San Francisco.
Place: Los Angeles County Medical Association Building, 1935 Wilshire Boulevard, Los Angeles.
Time: 6:00 P.M., fourth Monday of each month, September to May, incl.

AMERICAN OTORHINOLOGIC SOCIETY FOR THE ADVANCEMENT OF PLASTIC AND RECONSTRUCTIVE SURGERY.

President Dr. Romeo A. Luongo, 2054 Locust Street, Philadelphia.
Secretary: Dr. Jacob Daley, 104 East 40th Street, New York.



Central Institute for the Deaf

NATIONAL RESIDENTIAL AND DAY SCHOOL FOR THE DEAF AND DEFECTIVES IN SPEECH

Approved by Advisory Council of Foremost Ear Specialists and Educators

New fire-proof buildings beautifully located opposite Forest Park. Modern Dormitories and Equipment. Best home environments. Pupils constantly in care of teachers or experienced supervisors.

ORAL SCHOOL FOR DEAF CHILDREN

C. I. D. offers all advantages of exclusively Speech Training and expert medical supervision for both Resident and Day Pupils.
Nursery School (2 years of age) through the Elementary Grades.

ACOUSTIC TRAINING FOR CHILDREN WITH RESIDUAL HEARING

Salvaging of Residual Hearing is a specialty of C. I. D. The Acoustic Method was created here. Group and individual hearing aids used for class instruction at all grade levels.

LIP-READING INSTRUCTION

Private and Class Instruction for Hard-of-Hearing Adults and Children.
Conversational Classes for advanced pupils. Speech conservation stressed.

CORRECTION OF SPEECH DEFECTS

Private and Class Instruction for children with normal hearing and delayed speech or defective speech.
Resident and Day Pupils (2 years of age through Elementary Grades)
Private Instruction for Adults.
Correction of Imperfect Phonation, Imperfect Articulation, Aphasia, Stuttering.

TEACHERS TRAINING COLLEGE

Two years of Training following a professional curriculum for applicants with adequate college qualifications. Graduates qualify for degrees of Bachelor of Science in Education or Master of Science in Education from Washington University. Graduates prepared to teach both the deaf and speech defective.

DR. MAX A. GOLDSTEIN, Founder - MISS JULIA M. CONNERY, Principal Emeritus

For further information address

DR. HELEN SCHICK LANE, Principal

818 S. KINGSHIGHWAY 10, ST. LOUIS, MO.

CONTENTS

ACOUSTIC TRAUMA OF THE ORGAN OF CORTI IN THE GUINEA PIG. M. H. Lurie, M.D.; H. Davis, M.D., and J. E. Hawkins, Jr., Ph.D., Boston - 375

THE PROGRESS OF AVIATION OTOLOGY IN WORLD WAR II. Lieut. Col. Paul A. Campbell, M.C., U.S.A. - - - - - - - - - - - - - 387

THE TREATMENT OF EPISTAXIS BY SCLEROSING INJECTIONS. Samuel L. Fox, M.D., Baltimore - - - - - - - - - - - - - - - - 398

THE USE OF A BROCHOSCOPE TO MAINTAIN AN AIRWAY. REPORT OF A CASE. Richard W. Hanckel, Jr., M.D., Charleston, S. C. - - - - 402

VONEDRINE (PHENYLPROPYLMETHYLAMINE). CLINICAL STUDY OF A NEW NASAL DECONGESTANT. J. S. Bumgardner, M.D.; L. D. Abernethy, M.D., and F. B. Zimmerman, M.D., Louisville - - - - - 408

RHINOLOGY IN CHILDREN. RESUME AND COMMENTS ON THE LITERATURE FOR 1943. D. E. S. Wishart, M.D., Toronto - - - - - - - 421

IN MEMORIAM.
SAMUEL IGLAUER, M.D., 1872-1944 - - - - - - - - - - - - 452